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PERIOPERATIVE OUTCOME AND COMPLICATIONS OF ROBOTIC VERSUS RETROPUBIC RADICAL PROSTATECTOMY.

Inaugural dissertation

to

Obtain a doctoral degree of the Faculty of Medicine of Kiel University

Presented by

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From

Saudi Arabia

2016

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Day of oral examination: 10th October, 2017

Approved for printing, Kiel, dated: 14th June 2017

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In the name of **ALLAH**, the most Beneficent, the most Merciful, the most Compassionate.

This thesis is dedicated to the soul of my mother, may Allah forgive her and grant her his highest paradise (Ameen).

And to my father, for his great role in my life and his numerous sacrifices, support and encouragement. By this work, I attempt to follow in my father's footsteps, who received his PhD degree in Electrical Engineering from Dresden University of Technology in 1971.

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List of abbreviations

ANNA	Artificial neuronal network analysis
AUA	American Urological Association
BMI	Body mass index
BPH	Benign prostatic hyperplasia
CAUTIs	Catheter associated urinary tract infections
CDC	Centres for Disease Control and Prevention
CT	Computer tomography
DIC	Disseminated intravascular coagulation
DRE	Digital rectal examination
DVT	Deep venous thrombosis
EAU	European Association of Urology
FDA	U.S. Food and Drug Administration
HAI	Healthcare associated infection
HB	Haemoglobin
HC	Hematocrit
HRQL	Health-Related Quality of Life
LRP	Laparoscopic radical prostatectomy
NRC	National Research Council in US
PCa	Prostate cancer.
PCN	Percutaneous nephrostomy
PLND	Pelvic lymph node dissection
PSA	Prostatic specific antigen
RALP	Robotic assisted laparoscopic radical prostatectomy
RP	Radical prostatectomy.
RRP	Retopubic radical prostatectomy
SSI	Surgical site infection
TRUS	Trans rectal ultrasound
US	Ultrasound
U.S.A	United State of America
UTIs	Urinary tract infections
VAC	Vacuum Assisted Closure system
WHO	World Health Organization

1. Introduction:

1.1 The Prostate (Anatomy and function)

A firm, partly muscular, partly glandular body, the prostate is situated at the base of the male urethra; the average prostate weighs 18 g; measures 3 cm in length, 4 cm in width and 2 cm in depth; and is traversed by the prostatic urethra. Although ovoid, the prostate is referred to as having anterior, posterior and lateral surfaces, with a broad base superiorly that continues at the base of the bladder and a narrowed apex inferiorly at the urogenital diaphragm (the striated urethral sphincter). Its capsule is composed of collagen, elastin and abundant smooth muscle [1]. The prostate is composed of approximately 30% fibromuscular stroma and 70% glandular elements. The urethra does not run straight through the middle of the gland, but rather takes a curved course, running anteriorly as it proceeds from proximal to distal, in such a way that it ends up close to the prostate's anterior surface [2]. In the past, the prostate was described as having two lobes, with each lobe having its own ducts and in 1906, Howe described a middle (or median) lobe. This lobar concept was replaced in 1981 by McNeal with his concentric zones concept [3].

The transition zone, which accounts for 5–10% of the glandular tissue of the prostate, commonly gives rise to benign prostatic hypertrophy, which expands to compress the fibromuscular band into a capsule seen at enucleation of an adenoma. About 20% of prostate adenocarcinomas originate in this zone. *The peripheral zone* forms the bulk of the prostatic glandular tissue (70%) and covers the posterior and lateral aspects of the gland. About 70% percent of all prostatic cancers emerge from this zone and it is the zone most commonly affected by chronic prostatitis. The ducts of *the central zone* run circumferentially around the openings of the ejaculatory ducts and expand in a cone-like shape around the ejaculatory ducts to the base of the bladder. This zone constitutes 25% of the glandular tissue of the prostate and only 1% to 5% of adenocarcinomas arise in the central zone, although it may be infiltrated by cancers from adjacent zones [4]. Up to one third of the prostatic mass may be attributed to the non-glandular anterior fibromuscular stroma. This region normally extends from the bladder neck to the striated sphincter, although considerable portions of it may be replaced by glandular tissue in the adenomatous enlargement of the prostate [4].

The arterial supply of the prostate comes from the inferior vesical artery, the venous drainage of the prostate merges and runs through the periprostatic plexus and is drained into the internal iliac vein, the lymphatic drainage runs primarily towards the obturator and the internal iliac nodes; moreover, two neurovascular bundles are located on the postero-lateral side adjacent to the gland and form the superior and inferior pedicles on either side [2,4].

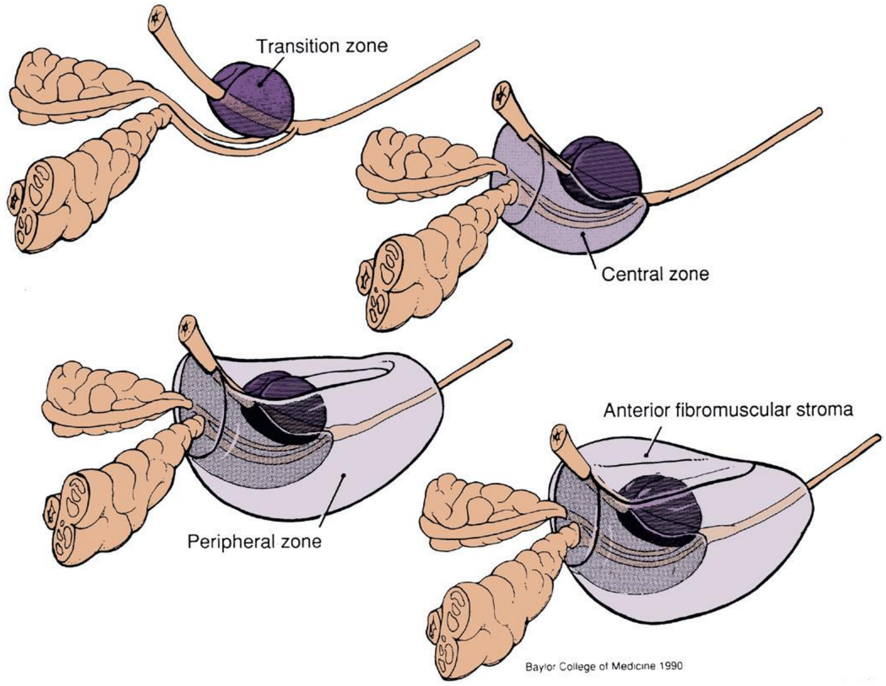

Figure 1: Zonal anatomy of the prostate as described by J.E. McNeal *(© 1990, Baylor College of Medicine.)*

The function of the prostate is to secrete a slightly alkaline fluid, milky or white in appearance, which in humans usually constitutes roughly 30% of the semen volume along with spermatozoa and fluid of the seminal vesicle. The alkalinity of semen helps neutralize the acidity of the vaginal tract, thus prolonging the lifespan of the sperm. The prostatic fluid is expelled in the first ejaculate fractions, together with most of the spermatozoa to provide better motility, longer survival and better protection of the genetic material [5].

1.2 Prostate cancer

1.2.1 Definition and epidemiology

Prostate cancer (PCa) is a malignant tumor of the prostate gland, which surrounds the urethra just below the bladder in front of the rectum and engenders fluid components of semen. Almost all prostate cancers are adenocarcinomas. It is the most prevalent cancer and the third most common cause of death due to cancer among men in Germany and the number of new cases has risen steadily in recent years; in 2010 there were 65,800 newly detected cases. PCa is rare in people under 50 years of age. For a 35-year old man, the risk of being diagnosed with PCa within the next ten years is lower than 0.1%, while for a 75-year old man it is approximately 6% [6].

1.2.2 Etiology

Although little is known about the causes of PCa development and the factors that influence its course, the presence of clustered cases among close relatives has now adequately been proved as a risk factor [6]. The results of a meta-analysis show that the relative risk increases with the number of affected family members, the degree of their relatedness and the age at which they are affected [7].

Chronic inflammation prompting cellular hyper-proliferation to supplant damaged tissue contributes to the development of infection-associated cancers of the colon, esophagus, stomach, bladder, liver and prostate [8,9]. In 1993 a possible relationship between vasectomy and PCa with a relative risk of 1.6 based on two large cohort studies was suggested for the first time [10,11]. Recently, a pooled relative risk of 1.37 was reported in a meta-analysis, with a linear trend suggesting a 10% increase for each additional 10 years since vasectomy [12]. Cigarette smoking, high fat consumption, especially of polyunsaturated fats, obesity and alcohol intake are considered as further risk factors for PCa [13–15].

1.3 Diagnosis

1.3.1 Symptoms

PCa rarely causes symptoms at an early stage. The presence of symptoms suggests locally advanced or metastatic disease. Locally advanced PCa may come with obstructive urinary symptoms, hematospermia or decreased ejaculate volume and rarely renal failure due to ureteral obstruction. Manifestations of metastatic disease include bone pain, pathologic fractures, anemia and lower extremity edema and less commonly, malignant retroperitoneal fibrosis, paraneoplastic syndromes and disseminated intravascular coagulation (DIC). Locally advanced and metastatic disease is less frequent due to widespread screening with prostate-specific antigen (PSA) and/or digital rectal examination (DRE) [16].

1.3.2 Digital rectal examination.

PCa is generally suspected on the basis of DRE and/or the level of PSA. However, conclusive judgment relies on the histopathological confirmation of malignancy in prostate biopsy cores or surgically extracted specimens [17]. PCa is detected by a suspect DRE alone, irrespective of the PSA level, in about 18% of all PCa patients [18]. A suspect DRE in patients with a PSA level of up to 2 ng/mL has a positive predictive value of 5-30% [19].

1.3.3 Screening

Population or mass screening is defined as systematic examination of asymptomatic men (at risk) with the principal goal to improve the overall health outcomes by identifying and treating disease at an earlier stage. However, screening is associated with many disadvantages, such as overdiagnosis and overtreatment. So early PSA-testing should be offered to men at an elevated risk of PCa., men over 50 years of age, men over 45 years of age and a family history of PCa and men with a PSA level of > 2 ng/mL at 60 years of age [20].

1.3.4 Prostatic specific antigen

PSA belongs to the human kallikrein gene family; it is secreted in high concentrations (ng/mL) in the seminal fluid and circulates in bound (complexed) and unbound (free) forms that can be measured using assays approved by the USA Food and Drug Administration (FDA) [16]. High and rising PSA levels are an indicator of possible development of PCa. Despite this, men may harbor PCa despite having low serum PSA; this was underscored by Thompson in 2004 who reports that the incidence of the presence of PCa in patients with PSA levels between 3.1-4.0 ng/mL is 26.9% [21]. Several modifications of serum PSA value that may improve the specificity of PSA in the early detection of PCa have been described. They include: PSA density; PSA density of the transition zone; age-specific reference ran ges, PSA velocity and doubling time and free/total PSA ratio [16].

1.3.5 Transrectal ultrasound examination and prostatic biopsy

prostate biopsies (PBs) is determined in case of a suspicious PSA level and/or a suspicious DRE [17]. A single increased PSA-value should not prompt an immediatebiopsy; instead the PSA level should be established again after a couple of weeks under cleary defined conditions (i.e. no ejaculation, no manipulations such as catheterization, no cystoscopy or transurethral resection and no urinary tract infection) in the same diagnostic laboratory and by using the same method [22,23]. PBs under ultrasound guidance is considered a standard approach. Although in general, a transrectal access is used for most prostate biopsies, some urologists prefer a perineal approach (Table 1). Cancer detection rates with perineal PBs are comparable to those obtained with transrectal biopsies, however many studies show that the transperineal approach has enhanced the identification of cancers in the transition zone sometimes not detected by the standard transrectal PBs in high-risk PCa patients [24–26].

1.3.6 The ANNA/C-TRUS system

Conventional grey scale ultrasound has only limited value in PCa diagnostics. The ANNA/C-TRUS system was developed to remedy this problem. It is based on an artificial neuronal network analysis (ANNA) of transrectal grey scale ultrasound pictures. The system was trained to identify the lesion most suspicious for PCa by coding it in different shades of yellow to red based on the analysis of targeted biopsies of suspicious lesions can be performed (Table 1) [27].

1.3.7 HistoScanning™

HistoScanning is a new non-invasive tissue characterization technology based on three-dimensional (3D) ultrasound, providing computer-aided analysis of the native ultrasound radiofrequency data to identify patterns in the glandular tissue in order to detect differentiated tissue [28]. Due to its special capacity to precisely distinguish, locate and assess the size of differentiated prostate tissue and augmented ultrasound analysis, it improves the interpretation of transrectal prostate imaging by identifying abnormal prostatic tissue (Table 1). Prostate HistoScanning may be used to guide clinical decisions throughout entire PCa care: detection and diagnosis, treatment planning, treatment guidance and post-treatment monitoring [29].

1.3.8 Magnetic resonance imaging (MRI) and fusion biopsy

There is growing interest in the use of prostate magnetic resonance imaging (MRI) to determine who should be offered PB and how those biopsies should be taken. The aim of using MRI to refine the biopsy strategy is to maximize the detection of clinically significant PCa, while reducing the burden of biopsy for patients and the health care system [30]. MRI is not only capable to assess PCa functionally and morphologically, in addition, local preoperative staging with conventional MRI was correct in 83.9%, with a better delineation of the prostatic capsule and early detection of infiltration into the neurovascular bundle [31]. The

BiopSee® PBs system is a novel development in this field by Hadaschik, 2011, integrating pre-interventional MRI data with peri-interventional US for perineal PB [32].

1.3.9 Computed Tomography (CT) and Positron Emission Tomography (PET)

The use of computed tomography (CT) to evaluate the local extent of disease and the possibility of nodal involvement is not routinely recommended due to low sensitivity; however, it may be used for detection of metastasis [33]. PET is a nuclear functional imaging technique that produces a three-dimensional image of the body and is often accomplished with the aid of a CT X-ray scan performed on the patient in the same session and with the same machine [34]. PET/CT used for the detection of lymph node (LN) involvement, bone metastases, local recurrence and distant metastases in cases of biochemical recurrence (BCR), particularly in intermediate to high-risk Pca patients, may also play a role in radiotherapy dose escalation or salvage therapy, particularly in salvage surgical treatment of LN metastasis (Table 1) [35,36]. There are many types of PCT/CT; 18F-FDG, the most commonly used radiopharmaceutical for PET in oncology is based on 2-[18F]fluoro-2-deoxy-d-glucose, also called fluorodeoxglucose or FDG and it is successfully used in many tumor types, [11C]-Choline-PET/CT is advisable in PMR cases with PSA levels of 1 ng/mL or higher [37].

1.3.10 Bone scans or bone scintigraphy

Bone scintigraphy is a nuclear scanning test to find certain abnormalities in the bone. It is primarily used to help diagnose a number of conditions relating to bones, including cancer of the bone or cancers that have spread (metastasized) to the bone, especially in PCa as more than 90% of the patients with advanced Pca develop bone metastases [38]. The sensitivity of bone scintigraphy to detect bone metastasis lies at about 94.1% and specificity at 89.2% [39].

Table 1: *Summary of sensitivity and specificity of the imaging diagnostic tools of Pca and metastasis.*

	Sensitivity	Specificity
TRUS	• 15-68% [40,41]	• 63-97% [40,41]
The ANNA/C-TRUS	• 83% [27]	• 64% [27]
HistoScanning™	• 82.1% [42] • 95% [28]	• - • -
MRI **MRI/ BiopSee®**	• 54.5% [31] • 98.5% [32]	• - • -
CT/PET • F-18 choline • 11C-choline • F-18 choline • F-18 choline	 • 79% [43] • 80% [44] • 83.3% [45] • 85.2% [36]	 • 97% [43] • - • 92.3%[45] • 18.2% [36]
bone scintigraphy	• 94% [39]	• 89%

1.4 Histopathology and Gleason Score

1.4.1 Histopathology

The vast majority of prostatic cancers are acinar adenocarcinomas. Histological variants of prostatic carcinoma have been variably defined. Acinar adenocarcinoma variants were defined in 2004 by the WHO to include atrophic, pseudohyperplastic, foamy, colloid, signet ring, oncocytic and lymphoepithelioma-like carcinomas. The second group of non-acinar prostatic carcinoma accounts for about 5–10% of carcinomas that originate in the prostate. These include sarcomatoid carcinoma, ductal adenocarcinoma, urothelial carcinoma, squamous and adenosquamous carcinoma, basal cell carcinoma and neuroendocrine tumours, specifically small-cell carcinoma [46].

1.4.2 Gleason score

The Gleason system is based on the glandular pattern of the tumor as identified at a relatively low magnification. Both the primary (predominant) and the secondary (second most prevalent) architectural patterns are identified and assigned a grade from 1 to 5, with 1 being the most differentiated and 5 being the least differentiated [47]. As both the primary and the secondary patterns affect the prognosis of PCa, there is a Gleason sum or score obtained by the addition of the primary and secondary grades [48].

1.5 Classification and staging systems

1.5.1 Table 2: *Tumor Node Metastasis (TNM) classification of PCa [49].*

T - Primary tumour	
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
T1	Clinically inapparent tumour not palpable or visible by imaging
T1a	Tumour incidental histological finding in 5% or less of tissue resected
T1b	Tumour incidental histological finding in more than 5% of tissue resected
T1c	Tumour identified by needle biopsy (e.g. because of elevated prostate specific antigen (PSA) level)
T2	Tumour confined within the prostate[1]
T2a	Tumour involves one half of one lobe or less
T2b	Tumour involves more than half of one lobe, but not both lobes
T2c	Tumour involves both lobes
T3	Tumour extends through the prostatic capsule[2]
T3a	Extracapsular extension (unilateral or bilateral) including microscopic bladder neck involvement
T3b	Tumour invades seminal vesicle(s)
T4	Tumour is fixed or invades adjacent structures other than seminal vesicles: external sphincter, rectum, levator muscles, and/or pelvic wall
N - Regional lymph nodes[3]	
NX	Regional lymph nodes cannot be assessed
N0	No regional LN metastasis
N1	Regional LN metastasis[4]
M - Distant metastasis[5]	
MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis
M1a	Non-regional lymph node(s)
M1b	Bone(s)
M1c	Other site(s)

1 Tumour found in one or both lobes by needle biopsy, but not palpable or visible by imaging, is classified as T1c.
2 Invasion into the prostatic apex, or into (but not beyond) the prostate capsule, is not classified as pT3, but as pT2.
3 The regional lymph nodes are the nodes of the true pelvis, which essentially are the pelvic nodes below the bifurcation of the common iliac arteries.
4 Laterality does not affect the N-classification
5 When more than one site of metastasis is present, the most advanced category should be used.

1.5.2 Risk classification of PCa

Table 3: *EAU risk groups for BCR of localized and locally advanced Pca, 2015 [50].*

	Low-risk	Intermediate-risk	High-risk	
PSA level	≤ 10 ng / mL and	10 – 20 ng / mL and	> 20 ng / mL or	any PSA
Gleason score	≤ 6 and	7a or 7b Or	> 7 or	any and
T- stage	T1a- T2a	T2b	T2c	T3-4 or N1
	Localised			***Locally advanced***

1.6 Treatment of localized PCa

1.6.1 Active surveillance and watchful waiting

Active surveillance aims to achieve correct timing for curative treatment; patients remain under close surveillance and are treated promptly on reaching a predefined threshold indicating potentially life-threatening disease, while considering the individual patient's life expectancy. Watchful-waiting refers to conservative management until development of local or systemic progression with disease-related complaints. At that point patients are treated palliatively with TURP or other procedures for urinary tract obstruction and hormonal therapy or radiotherapy for palliation of metastatic lesions [51].

Table 4: *Definitions of active surveillance and watchful waiting [52–54].*

	Active surveillance	**Watchful waiting**
Treatment intent	Curative	Palliative
Follow-up	Predefined schedule	Patient-specific
Assessment/markers used	DRE, PSA, re-biopsy, optional MRI	Not predefined
Life expectancy	> 10 years	< 10 years
Aim	Minimise treatment-related toxicity without compromising survival	Minimise treatment-related toxicity
Comments	Only for a subgroup of low-risk patients	Can apply to patients with all stages

1.6.2 Radical prostatectomy

radical prostatectomy (RP) is the surgical treatment of PCa, which has been performed for more than 100 years [55]. This includes the removal of the entire prostate gland and excision of both seminal vesicles, along with sufficient surrounding tissue to achieve a negative margin. Often, this procedure is accompanied by bilateral PLND [17]. It is considered a gold standard treatment of PCa owing to the realization that hormone therapy and chemotherapy are never curative and that not all cancer cells can be eradicated consistently by radiation or other physical forms of energy, even if the tumor is confined in the prostate gland [56,57].

The optimal outcome after RP for clinically localized PCa is freedom from BCR along with the recovery of continence and erectile function, a so-called *trifecta* [58]. Recently perioperative complications and positive surgical margins have been added to assess the success of the RALP, which called *pentafecta* [59].

1.6.2.1 Open radical prostatectomy

Perineal RP was initially performed in 1869 by Buchler and popularized in the United States by Young in 1905 [55]. In 1947, Millin was the first to describe the retro-pubic approach to RP and the morbidity of RP was reduced substantially after several detailed anatomic studies performed in fetal and adult cadavers in the late 1970s and early 1980s provided critical insight into the periprostatic anatomy, especially that of the dorsal vein complex, the neurovascular bundle and the striated urethral sphincter [60–62].

1.6.2.2 Laparoscopic radical prostatectomy

Schuessler and colleagues (1997) performed the first successful laparoscopic radical prostatectomy (LRP). At that time, several European teams added to the overall experience with this technique, with slowly rose in popularity and soon became a widespread minimally invasive alternative to RP, to the extent that many centers considered it as the approach of choice for the treatment of the localized PCa due to its advantages, such as the lower blood loss and transfusion rate associated with the laparoscopic approach, together with shorter hospital stay, reduced catheterization time, better pain control and the faster return to everyday activities [63].

1.6.2.3 Robotic assisted laparoscopic radical prostatectomy (RALP)

The first case was reported in 2000, thus ushering in a new era of minimally invasive surgery [64]. Da Vinci robot offered numerous advantages as it was capable of overcoming several of the obstacles present in laparoscopic surgery by providing improved visualization, increased dexterity, restored proper hand-eye coordination and an ergonomic position for the surgeon. Additionally, the system offers a 3D-image with a 12-foldmagnification (contingent upon the distance from the tissue), thus providing views that allow meticulous dissection to be performed. Since the camera is controlled by the surgeon, he or she can always maintain a stable, optimal view of the surgical field without concern for exhaustion of the camera-driver as in conventional laparoscopy [65]. Despite these well-recognized benefits, the current robotic platforms are not without profound drawbacks. Most outstandingly, the cost of acquiring and maintaining this new technology can be prohibitive [66]. Despite this, RALP has virtually replaced LRP in many centers in the world and the overwhelming majority of new surgeons have adopted RALP as their preferred surgical approach for PCa [67].

1.6.2.4 Complications of radical prostatectomy

Mortality and morbidity remain primary methods for assessing advantages and disadvantages of different surgical techniques and approaches. The incidence of postoperative complications is most frequently used as marker of surgical quality [68]. Therefore, measurement of morbidity requires an accurate definition of a surgical complication, which is defined as ''*an undesirable, unintended and direct result of an operation affecting the patient which would not have occurred had the operation gone as well as could reasonably be hoped*.'' [69,70].

In 2004, Dindo et al. presented a classification of surgical complications utilizing five grades containing seven levels (Table 5) [71]. This adjustment was implemented to add more precision and depend on whether an intervention due to the complication preformed under general anesthesia or not, admission to intensive care unit or not, occurrence a single or multiple-organ failure, which based on the type of therapy required to treat the complication. This modified classification, which is known as the Clavien- Dindo system, has widely been used in recent years by urologists [69].

Table 5: *The Clavien - Dindo classification of surgical complications.*

Grade	Definition
Grade I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics, electrolytes and physiotherapy. This grade also includes wound infections opened at the bedside
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications Blood transfusions and total parenteral nutrition are also included
Grade III	Requiring surgical, endoscopic or radiological intervention
Grade IIIa	Intervention not under general anesthesia
Grade IIIb	Intervention under general anesthesia
Grade IV	Life-threatening complication (including CNS complications)* requiring IC/ICU management
Grade IVa	Single organ dysfunction (including dialysis)
Grade IVb	Multi-organ dysfunction
Grade V	Death of a patient
If the patient suffers from a complication at the time of discharge the suffix “d” (for “disability”) is added to the respective grade of complication. This label indicates the need for a follow-up to fully evaluate the complication.	Suffix “d”

*Brain hemorrhage, ischemic stroke, subarrachnoidal bleeding, but excluding transient ischemic attacks. CNS, central nervous system; IC, intermediate care; ICU, intensive care unit.

RP is considered one of the major surgical interventions in the field of urology and similar to other major surgeries, complications may occur; these can be intraoperative complications e.g hemorrhage usually arising from venous structures, as well as vascular, intestinal, rectal, bladder, and/or ureteral injuries. Early postoperative complications include: hemorrhage, urinary leak or fistula, thrombo-embolic and cardiovascular events, urinary tract infection, lymphocele and wound problems and late complications may consist in erectile dysfunction, urinary incontinence, inguinal hernia and urethral stricture [56].

Surgical site infections (SSIs) are the most common health associated infections and present a problem in all surgical fields accounting for 2-5% of surgical complications in the United States [72]. This remains a major limiting factor for advancing the horizons of surgery despite the progress made in surgical control and SSIs continue to present a major cause of morbidity and extended hospital stay as well as aneconomic burden to the health care systems [73].

SSI is defined as an infection at or near the site of the surgical incision within 30 days of an operative procedure or where implants have been placed; this time period can be extended to 1 year if the infection appears to be related to the procedure [74].

Four classes of surgical wounds have been described: clean, clean-contaminated, contaminated and dirty (Table 6) [75]. The simplicity of this classification system has resulted in widespread use to predict the rate of infection after surgery.

Table 6: *Classification of surgical wounds according to the extent of microbial contamination.*

Classification	Criteria
Clean	Elective, nonemergency, non-traumatic case, primarily closed; no acute inflammation; no break in aseptic technique; respiratory, gastrointestinal, biliary and genitourinary tracts not entered.
Clean-contaminated	Urgent or emergency case that is otherwise clean; elective opening of respiratory, gastrointestinal, biliary, or genitourinary tract with minimal spillage (e.g., appendectomy) not encountering infected urine or bile; minor aseptic technique break.
Contaminated	Non-purulent inflammation; gross spillage from gastrointestinal tract; entry into biliary or genitourinary tract in the presence of infected bile or urine; major break in aseptic technique; penetrating trauma <4 hours old; chronic open wounds to be grafted or covered.
Dirty	Purulent inflammation (e.g., abscess); preoperative perforation of respiratory, gastrointestinal, biliary, or genitourinary tract; penetrating trauma >4 hours old.

There are 3 different sorts of SSIs defined by the Centers for Disease Control and Prevention (CDC) [76]. According to these criteria, SSIs are classified as either incisional or organ/space; incisional SSIs are further sub-classified as superficial (involving only skin and subcutaneous tissue) and deep (involving underlying soft tissue). Table 7 further elaborates the CDC classification system, which has been widely adopted by surveillance and surgical staff. In Germany, there is an OP-KISS protocol to define and standardize data collection of the SSIs and analysis in order to obtain reference data for internal quality assurance and to find the relation between the number of actual SSIs and the number of infections expected, depend on the patient's risk factor [77].

Table 7: *Surgical Site Infections (SSIs) as classified by the Centers for Disease Control and Prevention.*

Superficial Incisional SSIs Infection occurs after the operation and infection involves only skin or subcutaneous tissue of the incision.
Deep Incisional SSIs Infection occurs after the operation if no implant* is left in place or within 1 year if implant is in place and the infection appears to be related to the operation and infection involves deep soft tissues (e. g, fascial and muscle layers) of the incision.
Organ/Space SSIs Infection occurs after the operation if no implant is left in place or within 1 year if implant is in place and the infection appears to be related to the operation and infection involves any part of the anatomy (e. g., organs or spaces), other than the incision, which was opened or manipulated during an operation.

Numerous risk factors influence the wound infection rate and thus the risk of developing SSIs in the postoperative period. These factors can be either patient-related (coincident remote site infections or colonisation, diabetes, cigarette smoking, systemic steroid use, obesity >20% ideal body weight and poor nutritional status), or surgery-related (emergency procedures, long procedure length, the use of non-absorbable sutures, foreign bodies, copious use of subcutaneous electrocautery, excessive blood loss and hypothermia) [74,76,78].

1.7 Issue and hypothesis

There are only few studies comparing the perioperative complication rates of RALP with those of the open surgical approach. Our department's policy is to assess the perioperative outcome by recording and categorizing the complications of RP according to the Clavien-Dindo classification. In doing so, we are trying to answer many questions, e. g. how we can optimize our surgical treatment of PCa and how we can avoid complications, which type of RP approach has the better perioperative outcome and the lower complications rate. Moreover, we assessed the applicability of the Clavien- Dindo classification for RP complications in our department. Therefore, we designed a retrospective study to evaluate the patients who underwent RP in the period of January 2011 to March 2015 at the Department of Urology and Pediatric Urology of the University Hospital Schleswig-Holstein, Campus Kiel, to find answers to the above issues.

2. Objectives:

2.1 To make a statistic analysis comparing the preoperative and operative parameters of RRP and RALP.

2.2 To determine and compare the incidence of postoperative complications within 3 months after RRP and RALP.

2.3 To determine whether the surgical approach influences the incidence of postoperative complications.

2.4 To evaluate the result of RALP as performed by surgeons not previously trained in conventional laparoscopy or radical prostatectomy and to analyze the learning curve.

3. Patients and Methods:

The data shown in this study reflect patients who were treated with RP, either RRP or RALP for a confirmed diagnosis of PCa, regardless of whether it was performed as a primary curative treatment or a salvage operation. A retrospective case series study was conducted to report and compare the perioperative outcome and complications after RP at the Department of Urology and Pediatric Urology of the University Hospital Schleswig-Holstein, Campus Kiel, in the period between January 2011 and March 2015.

3.1 The standard patient protocol in both groups (RRP and RALP):

i) Preoperative:

- The patients were admitted to our department the day before the operation to assess their fitness to undergo surgery and for laboratory investigation (complete blood picture and urine analysis).
- The co–morbidities are documented according to the ASA classification (American Society of Anesthesiologists)

ii) Operative:

- All operations were performed under general anesthesia. The operative data are recorded as follows: type of surgery, with or without extended LN dissection, with or without nerve-sparing procedures, duration of surgical intervention and surgical complication if applicable.

iii) Postoperative:

- Complete blood picture and abdominal ultrasound were performed between 6 and 24 hours postoperatively.
- The two intraoperative drains, easy flow in RRP and Robinson 21 French drain in RALP, were usually removed between the 3rd and the 5th postoperative day.
- Preoperative single-shot antibiotic and postoperative antithrombotic prophylaxis were administered.
- A cystogram was performed in both groups on the 7th postoperative day to assess the integrity of vesico-urethral anastomosis; the urethral catheter was removed if no leakage appeared in the cystogram.
- The patient was usually discharged from our department on the 8th postoperative day.

3.2 A descriptive statistical comparative analysis was performed regarding the following parameters:

i) Preoperative data:

- Age of the patient
- BMI
- ASA score
- Hemoglobin (HB) g/dl, Hematocrit (HC) in % and White blood cells (WBCs) x106/µl on the day before the operation.
- Preoperative PSA and prostatic volume.

ii) Operative data:

- Operative type (RRP or RALP)
- Pelvic Lymph Node Dissection (PLND) Yes/No
- Nerve-sparing surgery: Yes/No
- Operative time in minutes (min).
- Complications;
    1- Open conversion for RALP
    2- Vascular injuries: any intraoperative vascular injury, whatever its sequelae
    3- Rectal, bladder and ureteral injury

iii) Postoperative data:

- Hemoglobin (HB) g/dl, Hematocrit (HC) in % and White blood cells (WBCs) x106/µl were determined between 6 and 24 hours postoperatively.
- Oncological data:
    1- Pathological tumor stage (pT- stage).
    2- Pathological LN stage and number of LN removed.
    3- Gleason score
    4- Surgical margin (we considered the surgical margin as an indicator of the oncological outcome)
- Complications within 90 days after the operation:
    1- Hemorrhagic complications in the form of hemoperitoneum and/or pelvic hematoma
    2- Anastomotic insufficiency, which is considered to present if leakage is shown in the first postoperative cystogram

3- Urethral stricture or urinary retention, occuring within 3 months postoperativly and requiring intervention.
4- Lymphoceles, which treated conservatively or requiring intervention, either under local anathesia e. g radiologically guided drain insertion or under general ananthesia e. g laparoscopic peritoneal fenestration.
5- Postoperative ileus, requiring medical treatment or other form of intervention
6- Transfusion of blood or fresh frozen plasma (FFP)
7- Thrombo-embolic complications, diagnosed by radiological investigation, e. g. CT chest for pulmonary embolism or Doppler ultrasound for deep venous thrombosis (DVT).
8- Urinary tract infections, i.e any microbiologically proven bacterial infection of urine.
9- SSIs; such as wound erythema or cellulitis necessitating antibiotic therapy and/or surgical intervention.

- All hospitalization periods were calculated by including the preoperative day.
- Catheterization time was calculated in days from the operation day until the day of catheter removal.

3.3 Statistical analysis:

We performed a descriptive statistical analysis of pooled data by using:

- Mann-Whitney U Test was used to compare between medians; the independent *t*-test was used to compare the mean across the groups and the Chi-squared test and Fisher's exact test were used for categorical variables.
- Correlations between different items in our study were done using Spearman or Pearson correlation coefficient.
- Statistical significance was set at ($p<0.05$). All reported p values are two-sided.
- Statistical analyses were performed with the Statistical Package for Social Science (SPSS), version 21.0.

4. Results:

Throughout the period from January 2011 to March 2015, 285 patients underwent RP, either RRP or RALP, at our department; 187 (66%) of these patients underwent RRP and 98 (34%) underwent RALP (Fig. 2).

In January 2013, the first case of RALP was performed at our department; from this time the majority of the patients underwent RALP and as the numbers in RALP were increasing, the number of patients who underwent RRP decreased gradually down to just five cases in 2014; in 2015 all cases were done with RALP (Table 8).

The age distribution of men who underwent RALP shows that about 50% were aged 70-79 years; none of the patients was under 50 years or over 80 years old. In contrast, of the men who underwent RRP only 45% were aged 70-79 years , only 2% of the patients were aged 40 – 49 years and 1% was over 80 years old (Table 9 and Fig.3).

The cohort data in Table 10 show that the average age of men who underwent RP was 68.1 years, the average body mass index (BMI) was 27.2 kg/m^2, 68% of the patients were overweight or obese (Fig. 4), 72.4% of the men had ASA score II, the median of the preoperative prostatic specific antigen (PSA) was 8.1 ng/mL, more than the half (54.2%) of the patients had a PSA in between 4 and 10 ng/mL (Fig. 5), and an average preoperative prostatic volume of 42.9 cm^3.

The patients who underwent RALP were more likely to have nerve-sparing procedures (82.7% vs. 47.1%, $p < .0001$) (Fig.5) and had a longer operative time with (mean 331.3 min. vs. 269.5 min, $p < .0001$) (Fig.6). However, RALP caused less perioperative HC loss (mean 10.6% vs. 12.6%, $p = .033$) (Fig.8), lower catheterization times (mean 9.2 days vs. 12.6 days, $p < .0001$) and shorter mean hospitalization time (9.7 days vs. 13.5 days, $p < .0001$) (Fig.8). Almost all patients underwent LN dissections in both groups (Table 11).

The oncological data that are presented in Table 12 reveal a statistically significant difference between groups regarding pT sage, N stage and safety margins. More than 50% of the patients who underwent RP had a pathological tumor stage (pT_2), only 0.4% had pT_4 (Fig. 10) and more than 75% of the patients had LN metastases-free status (N0) (Fig. 11); more than 65% of the safety margins were negative (Fig. 12) and about 30% of the Gleason scores of removed PCa were 3+4= 7_a.

Table 13 summarizes the percentage of the incidence of postoperative complications for each group. In total, 285 patients underwent RP over the period of the last 4 years and we observed complications in 154 patients (54%) (Fig.12). A statistically significant differences between the groups were found regarding the total incidence of the postoperative complications (RALP 38.8% vs. RRP 62%, p = *.001*) (Fig.13), anastomotic insufficiency (RALP 10.2% vs. RRP 20%, p =. *024*) and hemorrhagic complications (RALP 4% vs. RRP 0.5%, p =*.033*) (Fig.14).

The presented data in Table 14 classify the complications according to the Clavien-Dindo Classification and show that about one third (34%) of the patients had minor complications (Clavien-Dindo Classification I and II) and about 16% of the patients had major complications (> Grade II, Fig. 16).

Thus, we observe from this statistical analysis that;

- The patients underwent RALP were more likely to have nerve-sparing procedures, on the other hand longer operative timewas longer.
- The patients who underwent RALP had a shorter catheterization and hospitalization time.
- The patients who underwent RALP had negative surgical margins more often.
- The patients who underwent RALP had lower complications rates in all modified Clavien-Dindo classes than those who underwent RRP.
- The patients who underwent RALP had a lower incidence of anastomotic insufficiency and SSIs than those who underwent RRP.
- The patients who underwent RALP were more prone to haemorrhagic complications than those who underwent RRP.

4.1 Tables:

Table 8: *Number of surgeries performed in each calendar year.*

Years	RALP	RRP	Total
2011	-	81	81
2012	-	67	69
2013	30	32	62
2014	55	5	60
March, 2015	13	-	13
Total	98	187	285

Table 9: *Age distribution.*

Age: (years)	RALP	RRP	Total
40- 49	-	3	3
50-59	8	20	28
60-69	41	78	119
70-79	49	84	113
>80	-	2	2
Mean ± SD	68.9 ± 6	67.7 ± 6.9	68.1 ± 6.7

Table 10: *Preoperative data.*

	RALP	RRP	Total	*P value*
Total no. of cases	98	187	285	
Age at operation, yr.				
Mean [a]± SD	68.9 ± 6	67.7 ± 6.9	68.1 ± 6.7	.196
Median[b] (Range)	69.5 (51-79)	68 (47-85)	69 (47-85)	.203
BMI, kg/m^2,				
Mean [a]± SD	26.8 ± 2.9	27.3 ± 4	27.2 ± 3.8	.035
Median[b] (Range)	26.3 (22.1-34)	26.4 (19.5-42.4)	26.4 (19.5-42.4)	.672
BMI[c] , %				.154
Normal (18.5–24.9)	26.8	33.3	32	
Overweight (25–29.9)	61	44.8	48.1	
Obese (30 or greater)	12.2	21.8	19.9	
ASA[c] ,%				.517
I	1.9	5.3	4.4	
II	72.2	72.5	72.4	
III	25.9	22.2	23.1	
Preoperative PSA ng/mL, median [b]	7.4	8.7	8.1	.082
PSA[c] ng/mL, %				.003*
<4	4.1	9.7	7.7	
4 to < 10	68.4	46.8	54.2	
10 – 20	19.4	23.7	22.2	
>20	8.2	19.9	15.8	

Preoperative HB (g/dl)				.004*
Mean [a] ± SD	14.4 ± 1.4	14.6 ± 1	14.5 ± 1.2	
Median[b] (Range)	14.5 (10.1-17.2)	14.6 (10.6- 17.3)	14.6 (10.1- 17.3)	< .0001*
Preoperative HC %				
Mean [a] ± SD	41.7 ± 3.9	41.9 ± 3.9	41.8 ± 3.7	.104
Median[b] (Range)	42 (26- 49)	42 (15- 49)	42 (15- 49)	< .0001*
WBCs (x106/µl)				.1
Mean [a] ± SD	6.7 ± 2.9	6.7 ± 1.6	6.7 ± 2.2	
Median[b] (Range)	6.2 (1.8- 29.7)	6.5 (3.4- 12.1)	6.4 (1.7-29.7)	< .0001*
Prostatic volume, cm^3				
Mean [a] ± SD	45.4 ± 23.1	41.6 ± 20.1	42.9 ± 21.2	.279
Median[b] (Range)	40 (13-149)	37 (12-160)	38 (12-160)	.236

[a] Independent T- test
[b] Mann-Whitney U Test
[c] Chi-squared test
* Statistical significant difference (P < 0.05)

Table 11: *Perioperative data.*

	RALP	RRP	Total	*P value*
Cases no.	98	187	285	
Nerve sparing [c], %				< .0001*
Yes	82.7	47.1	59.3	
Lymph node dissection [c], %				.468
Yes	100	99.5	99.6	
Operative time, min				
Mean [a] ± SD	331.3 ± 57.1	269.5± 47.9	290.7 ± 58.7	< .0001*
Median [b] (Range)	321 (210- 503)	270 (150-450)	285 (150-503)	< .0001*
Catheterization time, days				
Mean [a] ± SD	9.2 ± 5.6	12.6 ± 10.2	11.4 ± 9	.001*
Median [c] (Range)	7 (6-36)	8 (6-69)	7 (6-69)	< .0001*
Hospitalization time, days				
Mean [a] ± SD	9.7 ± 3.4	13.5 ± 9.1	12.2 ± 7.9	< .0001*
Median [b] (Range)	9 (7-35)	10 (8-71)	9 (7-71)	< .0001*
HB loss g/dl				
Mean [a] ± SD	3.9 ± 1.8	4.4 ± 1.3	4.2 ± 1.5	.06
Median [b] (Range)	3.6 (0.3-13.4)	4.4 (0.6-8)	4.1 (0.3-13.4)	< .0001*
HC loss %				
Mean [a] ± SD	10.6 ± 4.7	12.6 ± 3.9	11.9 ± 4.3	.033*
Median [b] (Range)	10 (1-23)	13 (2- 24)	12 (1-24)	< .0001*
WBCs difference ($x10^6$/µl)				
Mean [a] ± SD	2.1 ± 2.7	2.8 ± 2.8	3.4 ± 2.9	.078
Median [b] (Range)	1.9 (-12.2 – 11.5)	2.8 (-2.3 – 19.8)	3.4 (-12.2 – 19.8)	< .0001*

[a] Independent T- test
[b] Mann-Whitney U Test
[c] Chi-squared test
* Statistical significant difference (P < 0.05)

Table 12: *Oncological outcome.*

	RALP	RRP	Total	*P value*
pT stage [c], %				.022*
T2	68.4	54.3	59.2	
T3	30.6	45.7	40.5	
T4	1	0	0.4	
N stage[c], %				.001*
Nx	3.1	1.1	1.8	
N0	86.7	70.1	75.8	
N1	10.2	28.9	22.5	
Gleason score [c], %				.079
< 6	1	1.1	1.1	
6	23.5	21.6	22.3	
3+4	32.7	27.6	29.3	
4+3	28.6	20.5	23.3	
≥ 8	14.3	29.2	24	
No. Of lymph node removed				
Mean [a]± SE	15.6 ± 8.8	26.2 ± 10.6	22.6± 11.2	.113
Median [b] (Range)	15 (0-40)	25 (3-65)	22 (0-65)	< .0001*
Margins [c], %				< .0001*
Positive multiple	12.2	4.3	7	
Positive one	9.2	32.3	24.3	
Negative	78.6	63.4	68.7	

[a] Independent T- test
[b] Mann-Whitney U Test
[c] Chi-squared test

* Statistical significant difference (P < 0.05)

Table 13: *Number and percentage of the incidence of postoperative complication.*

	RALP	RRP	Total	P value	r value
Total of complicated cases: No. (%)	38 (38.8)	116 (62)	154 (54)	.001*	.058
Vascular injuries: No. (%)	3 (3.1)	0	3 (1.1)	.041*	.041
Rectal injury: No. (%)	1 (1)	3 (1.6)	4 (1.4)	.569	.054
Anastomotic insufficiency: No. (%)	10 (10.2)	37 (19.8)	47 (16.6)	.024*	.053
Hemorrhagic complications: No. (%)	4 (4)	1 (0.5)	5 (1.8)	.05*	.057
Postoperative urinary difficulty: No. (%)	1 (1)	1 (0.5)	2 (0.7)	.573	.063
Lymphocele: No. (%)	8 (8.1)	26 (13.9)	34 (11.9)	.102	.055
Thromboembolic complication: No. (%)	1 (1)	4 (2.2)	5 (1.8)	.434	.051
Urinary tract infections: No. (%)	2 (2)	5 (2.7)	7 (2.5)	.540	.057
SSIs: No. (%)	2 (2)	17 (9.1)	19 (6.7)	.001*	.179
Ileus: No. (%)	2 (2)	4 (2.2)	6 (2.1)	.656	.059
Transfusion: No. (%)	6 (6.1)	14 (7.6)	20 (7.1)	.426	.057
Uretric injury or stricture: No. (%)	0	2 (1.2)	2 (0.7)	.427	.022
Open Conversion: No. (%)	1 (1)	0	1 (0.4)	.465	.043
Death: No. (%)	0	2 (1.2)	0.7	.43	.022

Fisher's exact test

* Statistical significant difference (P < 0.05)

Table 14: *Numbers of the complicated cases according to modified Clavien-Dindo classification.*

Grade	Definition	RALP	RRP	No.	% to total no.
Grade I	▪ Leakage occurred in 35 cases after RRP and in 10 cases after RALP and was treated with ***prolonged catheterization***. ▪ One patient developed a ***subcutaneous hematoma due to RALP.*** ▪ 8 RRP cases and 2 RALP cases developed ***small lymphoceles***. ▪ 4 RRP cases and 2 RALP cases developed postoperative ileus. ▪ 3 RRP cases developed postoperative ***superficial SSIs.*** ▪ ***Open conversion occurred in one case during RALP***	**16**	**50**	**66**	**23.1**
Grade II	▪ 2 RRP cases of ***incomplete rectal injury*** discovered intraoperatively were treated with primary closure and postoperatively with total parenteral nutrition. ▪ 2 RALP cases and 5 RRP cases were diagnosed with a ***positive urinary culture*** of $>10^5$ colonies/mL urine and treated by intravenous antibiotics. ▪ 14 RRP cases and 6 RALP cases needed ***postoperative transfusion*** either erythrocyte concentrate, FFP and/ or platelet concentrate. ▪ 2 RRP cases developed postoperative ***DVT***, which were treated by anticoagulant therapy.	**8**	**23**	**31**	**10.8**
Grade IIIa	▪ ***Leakage***, in one case of RRP was treated by bilateral PCN under local anesthesia. ▪ 3 cases RRP and 3cases RALP presented with postoperative ***lymphoceles*** that were treated by US-/ CT-guided pig tail insertion under local anesthesia. ▪ 2 RALP cases presented with infected lymphoceles ***(space SSIs)*** that were treated by CT- guided pig tail insertion.	**5**	**4**	**9**	**3.1**
Grade IIIb	▪ In one RALP and one case RRP case, ***rectal injury was*** discovered intraoperatively and treated with primary closure and a safety proximal ileostomy that required closure after 6-8 weeks. ▪ In one case of RRP ***anastemotic insufficiency*** was detected requiring urethrocystoscopy to evaluate the anastomotic area under general anesthesia. ▪ In 3 RALP cases and one RRP case postoperative bleeding and ***pelvic or retroperitoneal hematoma occurred requiring*** immediate surgical evacuation under general anesthesia and/or bilateral immobilization of the internal iliac arteries. ▪ In one case of RALP and RRP each, ***difficulty of micturition*** developed within 3 months postoperatively; this was was treated by transurethral resection of the anastomotic area. ▪ 15 RRP cases and 3 RALP cases presented with postoperative ***lymphoceles*** that were treated by laparoscopic peritoneal fenestration. ▪ 13 RRP cases developed postoperative SSIs and wound dehiscence ***(Deep incisional SSIs)***, which were treated	**8**	**35**	**43**	**15.1**

	by regular exchange of the Vacuum-Assisted Closure system (VAC). ▪ One cases RRP presented by infected lymphocele ***(space SSIs)*** that treated by open surgical evacuation and lavage. ▪ One case RRP developed postoperative ***ureteric stricture*** that need re-exploration and re-implantation of the ureter into the bladder under general anesthesia. ▪ One case RRP was intraoperative ***ureteric injuries*** due to marked retroperitoneal fibrosis, which treated by primary closure and JJ stint was inserted and one month after the operation removed.				
Grade IVa	▪ One case RRP developed postoperative ***massive pulmonary embolism*** and was admitted in ICU. ▪ One case RRP and one case RALP developed postoperative ***cerebral stroke*** which treated anticoagulant therapy with development of neurological affections.	**1**	**2**	**2**	**0.7**
Grade IVb	▪ 0	**0**	**0**	**0**	**0**
Grade V	▪ Two cases.	**0**	**2**	**2**	**0.7**
		38	**116**	**154**	

4.2 Figures:

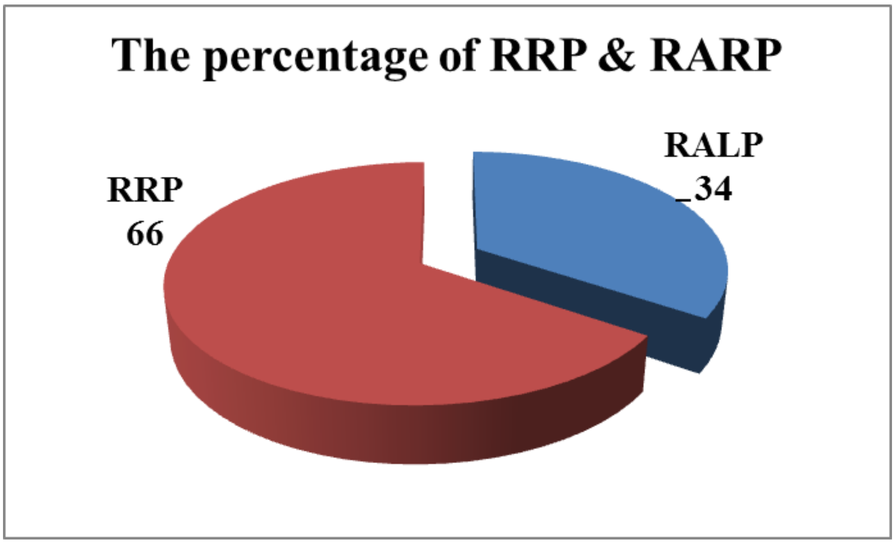

Figure 2: Percentage of RRP and RARP, %

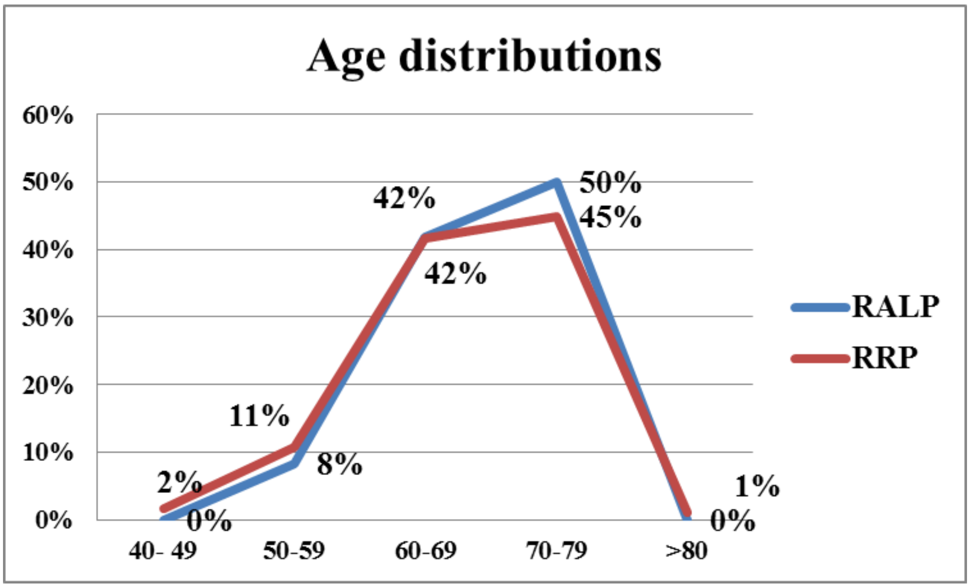

Figure 3: Age distribution in both groups

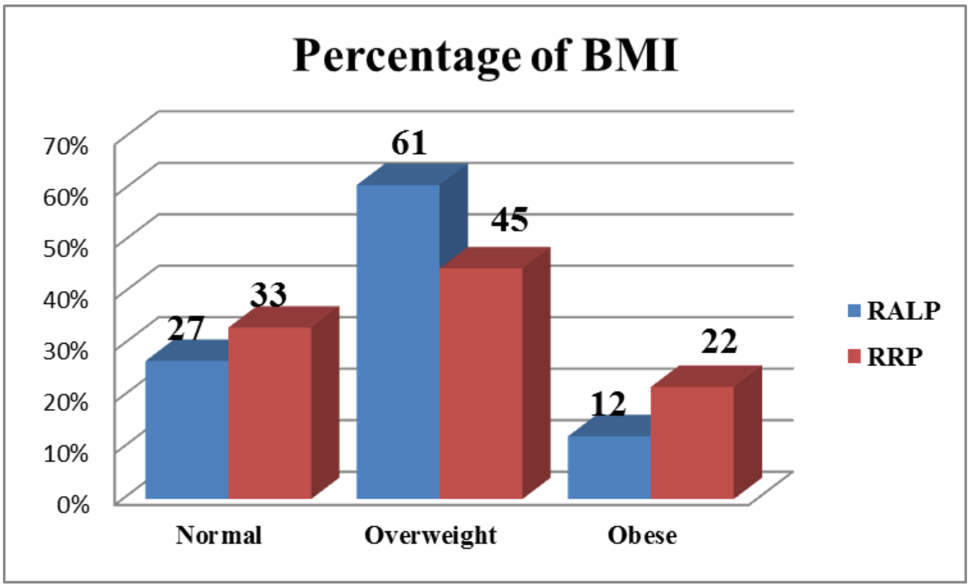

Figure 4: Percentage of BMI according to the surgical technique, %

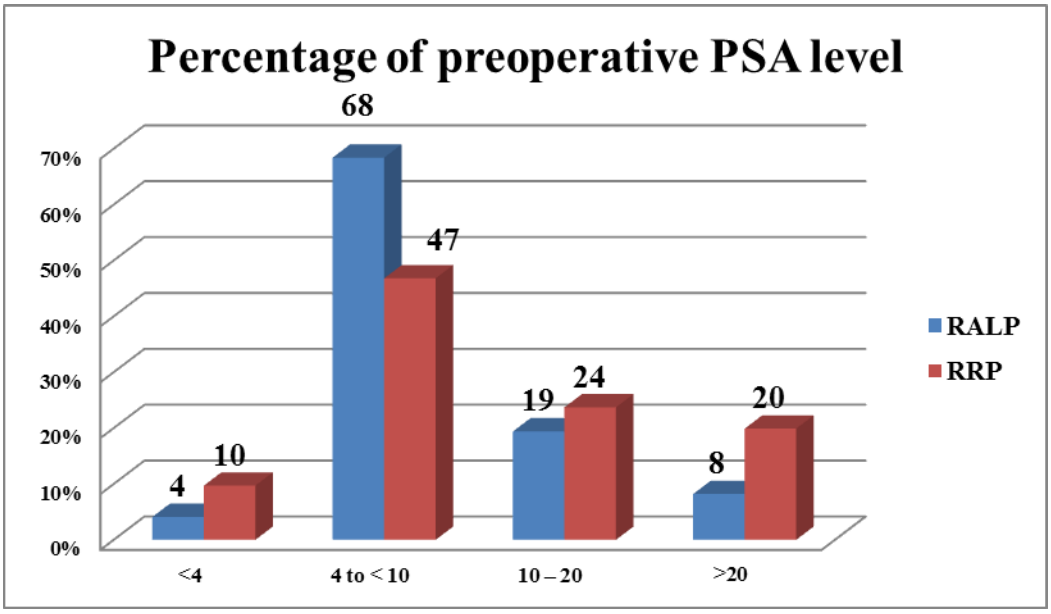

Figure 5: Percentage of preoperative PSA mg/dl, %

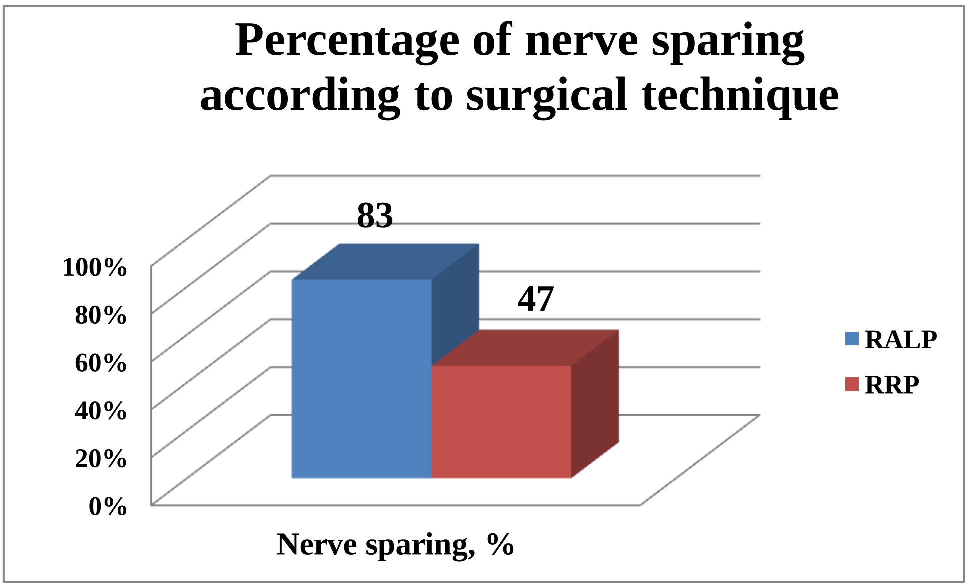

Figure 6: Percentage of nerve sparing according to surgical technique, %

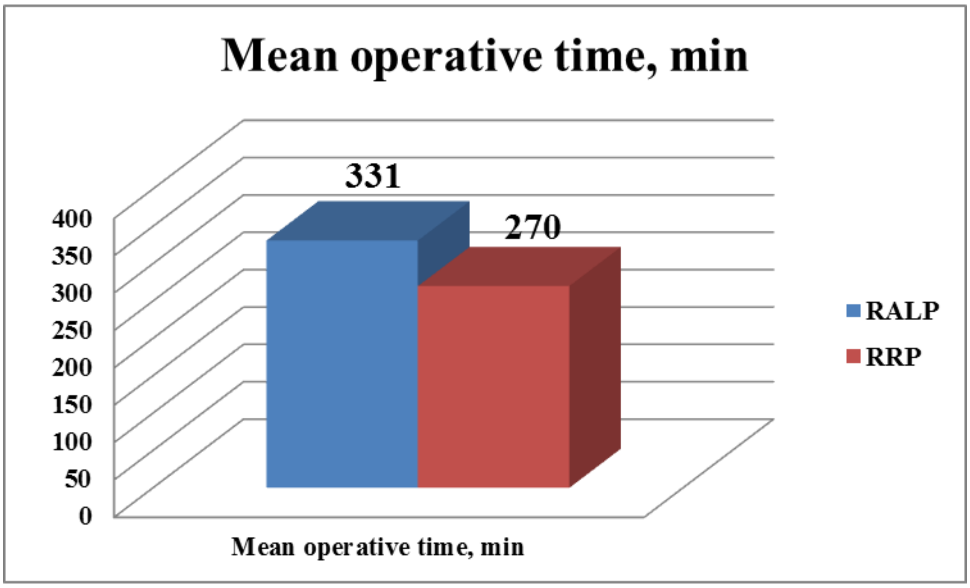

Figure 7: Mean operative time, min

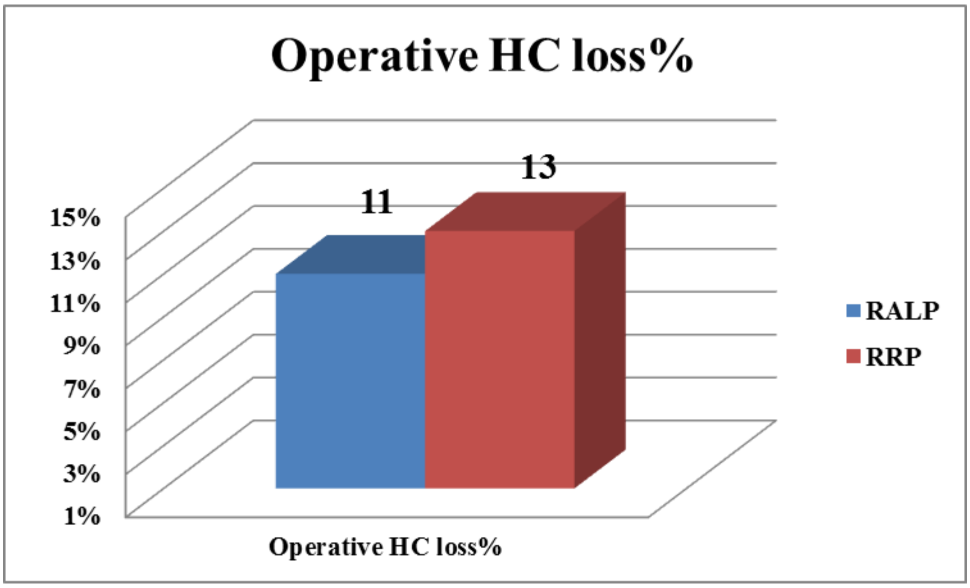

Figure 8: Mean operative HC loss, %

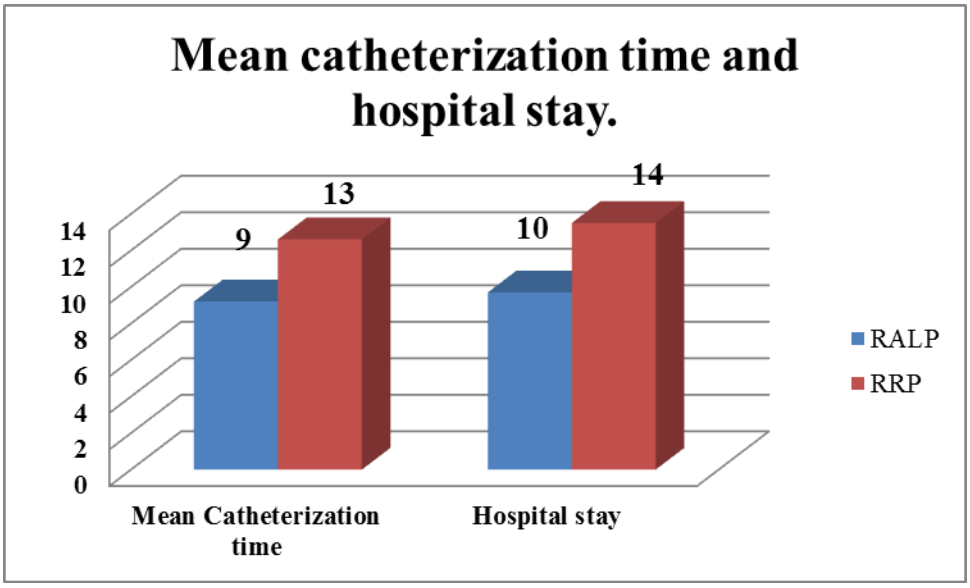

Figure 9: Mean catheterization time and hospital stay, days

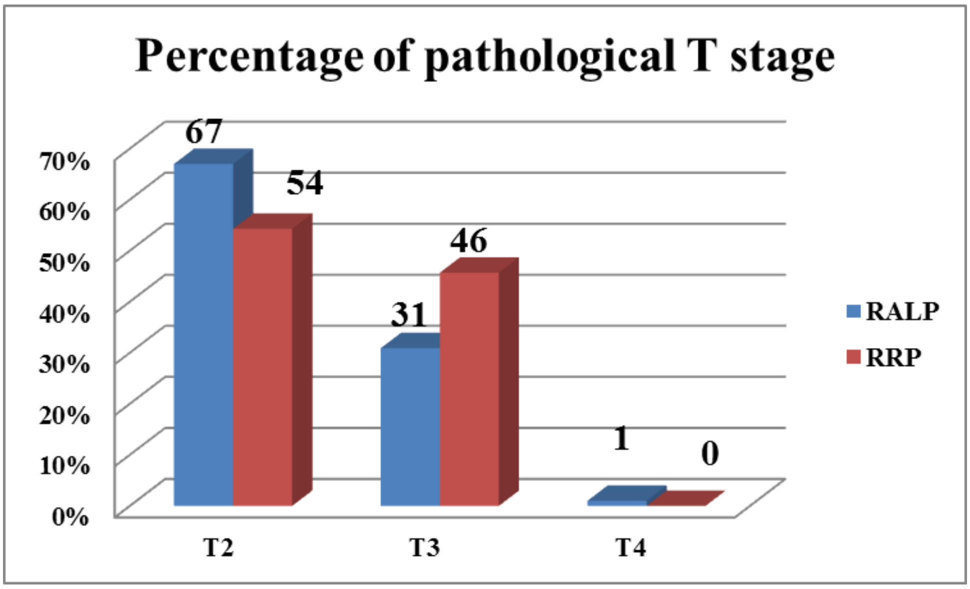

Figure 10: Percentage of pathological T stage, %

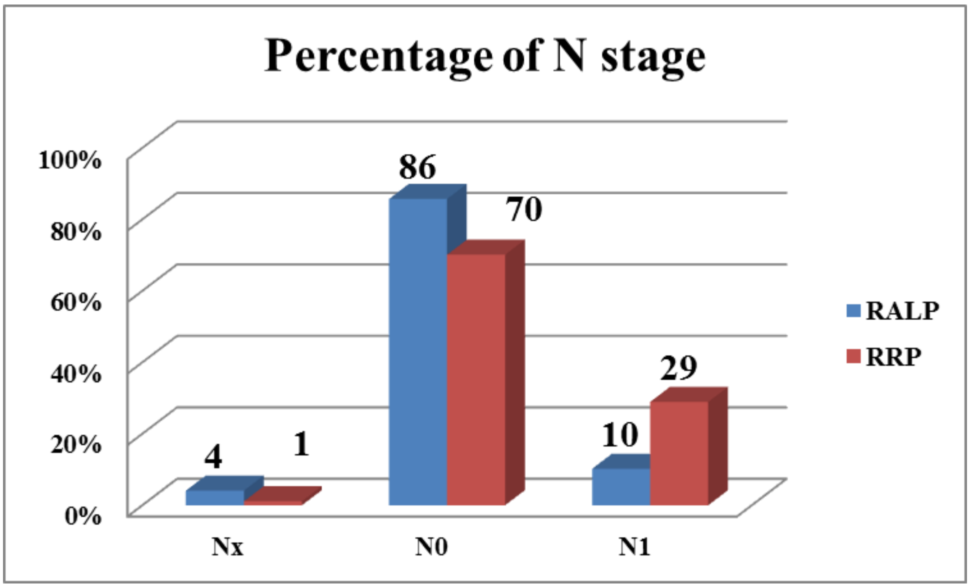

Figure 11: Percentage of N stage, %

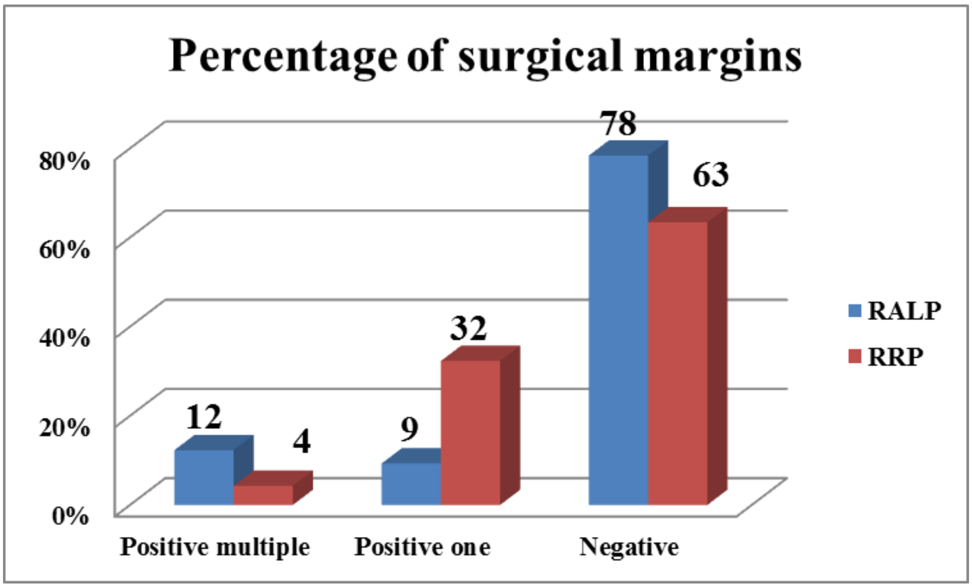

Figure 12: Percentage of surgical Margins, %

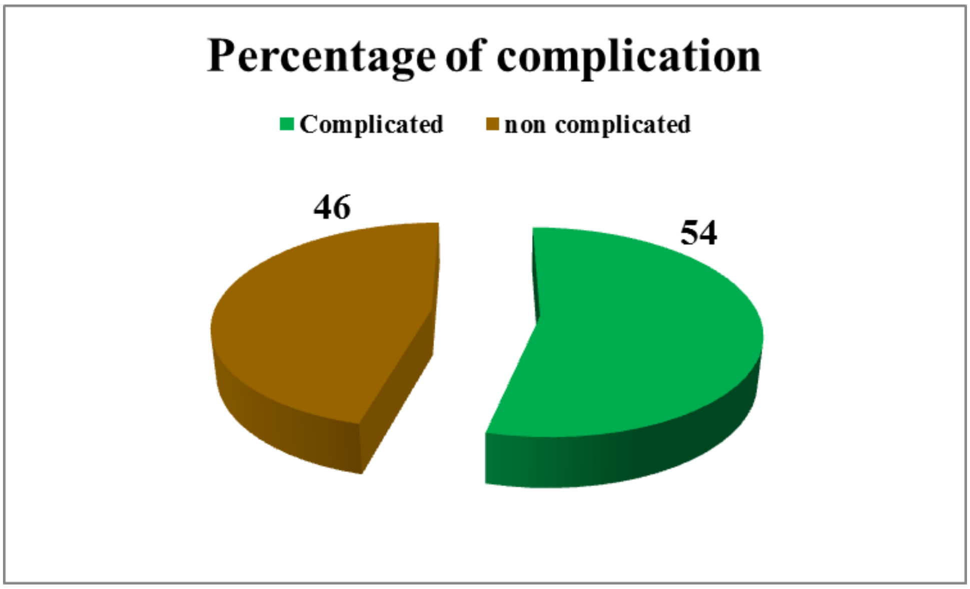

Figure 13: Total Incidence of complications, %

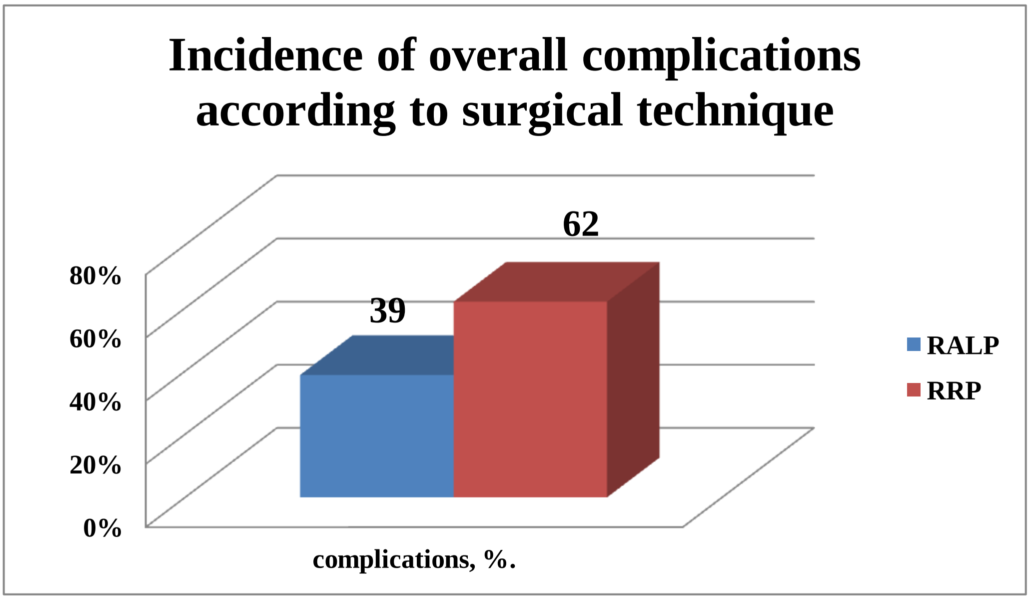

Figure 14: Incidence of complications according to surgical technique, %

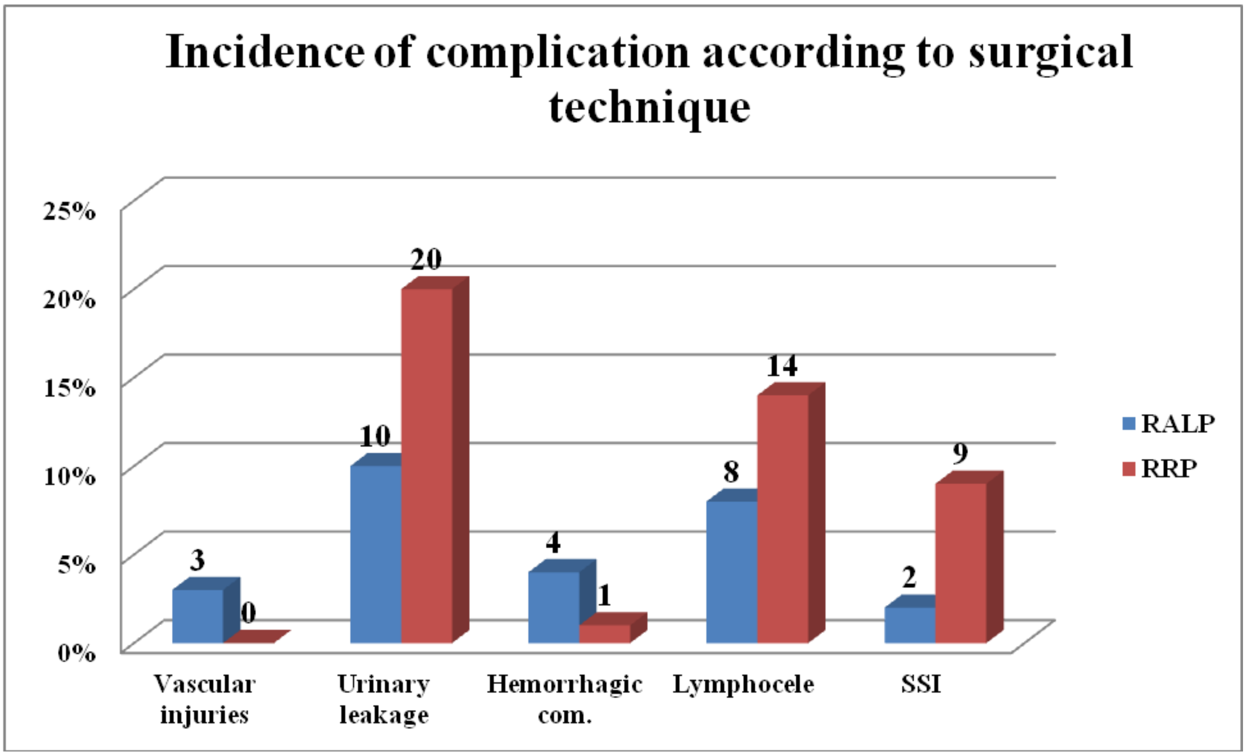

Figure 15: Incidence of complications in relation to surgical technique, %

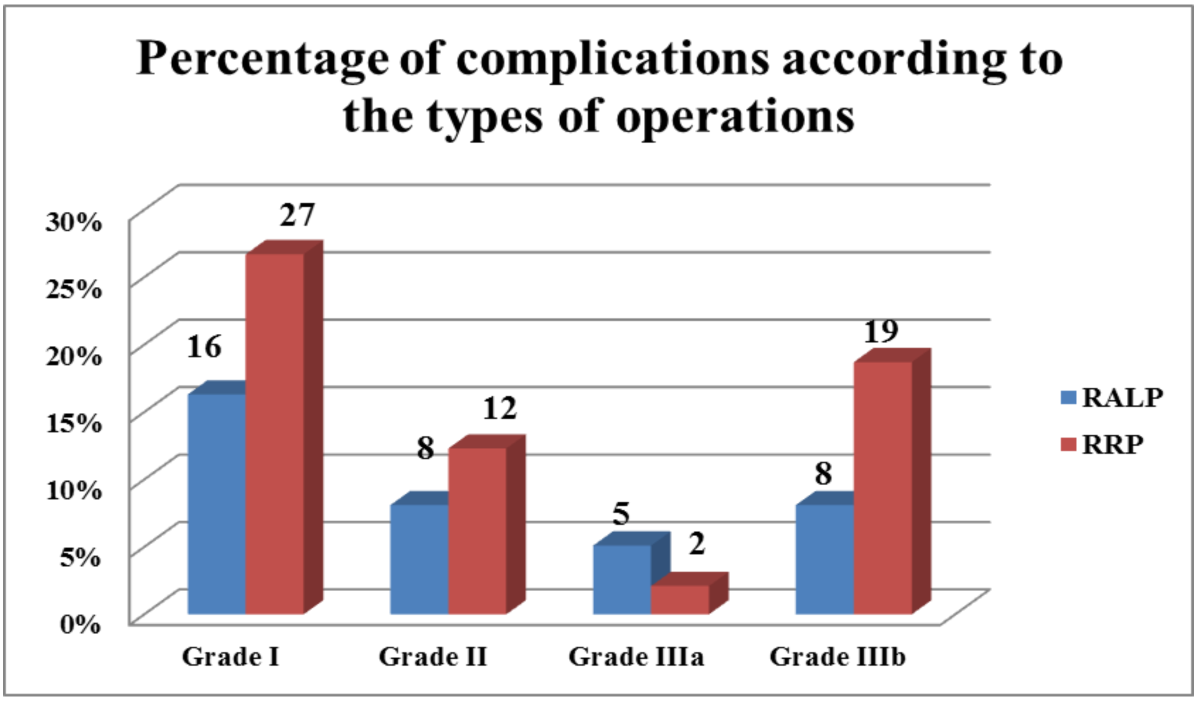

Figure 16: Percentage of complicated cases in relation to operation type and modified Clavien-Dindo Classification, %

5. Discussion:

For valid results, the ideal methodological setting for comparing RRP with RALP should be based on consistent surgical procedures performed at a single institution with a clearly defined surgical technique, grading complications and consistent pathological assessment [79]. For each surgical procedure, perioperative complications are the major indicators of surgical results, particularly in RP where different surgical approaches are available [80].

In this study we compared the short-term perioperative outcome (within 90 days postoperatively), with respect to the oncological and functional results and the complications rates of RALP versus RRP in a single institution. In doing so, we are also reporting and evaluating the experience of our center changing from the open approach to a robot-assisted approach. The open approach had been performed in a large volume of cases by two highly experienced surgeons without any laparoscopic experience; both started RALP at same time so that our data include a learning curve; our aim was to confirm that RALP could be accomplished by surgeons who had not previously been trained in conventional LRP and to determine whether this change of the surgical approach would influence the incidence of complications after RP.

This descriptive and retrospective study has some obvious limitations. Firstly, it is difficult to record all complications objectively as some colleagues only report major complications of vital importance and disregard minor complications. Secondly, the distinction between the different Clavien classification grades is sometimes unclear and the allocation to different complication grades underlies a certain degree of subjectiveness.

5.1 Preoperative data

5.1.1 Age

Between 1962 and 2002 the average life expectancy in the German population increased from 67.1 to 75.6 years in men and from 72.7 to 81.3 years in women with an average gain of approximately 2.2 years per decade in both genders [81]. Traditionally, RP used to be restricted to men with a life expectancy of 10 years or more and to cases with a localized PCa [17]. The median age of men that underwent RP in our study was 69 years at the time of surgery; these men generally had a life expectancy at least 10 years (Table 9 and Fig.3).

5.1.2 BMI

There is a solid relationship between obesity, diabetes, coronary artery disease, hypertension and additionally there is a significant impact on mortality in cancer patients, so it is a standout amongst the most pressing problems that the healthcare system is facing; an elevated BMI also plays a significant role in cancer progress, aggressiveness and even cancer-related mortality, especially in PCa, despite the fact that most studies cannot prove this correlation [82]. In our study, approximately 68% of the men had an elevated BMI (overweight and obesity) (Table 10 and Fig.4). There were a significant differences regarding catheterization time and hospitalization time in correlation with different BMI groups, which is generally in accordance with the data from randomized controlled trials evaluating the impact of BMI on perioperative outcomes (Table 15).

Table 15: *The impact of patients' BMI on the perioperative outcomes.*

First author	Institution	Cases	Operative time, min, median/mean	Catheterization duration, d	In-hospital stay, d
Wiltz, 2009[a][83]	University of Chicago, IL, USA	BMI < 25: 216	217 ± 58*	6 ± 1.1	1.2 ± 0.6
		BMI 25–30: 464	214 ± 65*	6 ± 1.3	1.2 ± 1.2
		BMI >30: 265	234 ± 77*	6 ± 1.8	1.2 ± 1.5
Moskovic, 2010[a][84]	Mount Sinai Medical Center, New York, NY, USA	BMI < 25: 270	121*	-	1.25*
		BMI 25–30: 600	122*	-	1.25*
		BMI >30: 242	126*	-	1.17*
Zilberman, 2011[a][85].	Duke University Medical Center, Durham, NC, USA	BMI < 25: 100	159(137-202)*	-	-
		BMI 25–30: 286	181 (151-220)*	-	-
		BMI 30- 34.9: 135	178 (148-230)*	-	-
		BMI >35: 34	191 (162-225)*	-	-
Our study [b]	Department of Urology and Pediatric Urology, University Hospital, Kiel, Germany.	BMI < 25: 66	283 ± 62	11 ±8*	12 ±.6*
		BMI 25–30: 99	286 ± 58	11 ± 7*	12 ±7*
		BMI >30: 41	281 ± 52	17 ± 14*	16 ± 14*

[a] These studies evaluate the impact of BMI on the perioperative outcome after RALP. * Statistically significant
[b] One way ANOVA

5.1.3 Prostatic volume

Many studies demonstrate that an increased prostate volume is associated with a longer operative time, catheterization and hospitalization times and a higher rate of complications but not with higher rate of positive surgical margins (PSMs) in RRP or LRP [86,87]. In a large RALP series, Link *et al* 2008 evaluated the impact of the prostate size in a series of 1847 cases, demonstrating greater blood loss, longer hospital stay and more complications (e. g., urinary leak) for larger-sized prostates [88]. Our results are comparable to these data (Table 16).

Table 16: *The impact of prostatic volume on the perioperative outcomes.*

First author	Institution	Cases	Operative time, min، median/mean	Catheterization duration, d	In-hospital stay, d
Link, 2008[a] [88]	City of Hope, Duarte, CA, USA	Prostate volume <30 cm^3: 69 Prostate volume 30–49 cm^3: 883 Prostate volume 50–69 cm^3: 568 Prostate volume >70 cm^3: 327	168 ± 42* 168 ±42* 180 ± 48* 192 ± 48*	6 (6–8)* 6 (6–8)* 6 (6–8)* 7 (7–8)*	- - - -
Allaparthi, 2010[a] [89]	Turfts University, Brighton, MS, USA	Prostate volume <30 cm^3: 10 Prostate volume 30–49 cm^3: 182 Prostate volume 50–79 cm^3: 91 Prostate volume >80 cm^3: 12	129 ± 28 127 ±20 128 ± 3 127 ± 20	2± 2.7 1 ± 0.7 - -	1 1.2 (1-12) 1(1-2) 1.4(1-5)
Martinez, 2010[a] [90]	University of Western Ontario، London, Ontario, Canada	Prostate volume <40 cm^3: 75 Prostate volume 40–60 cm^3: 51 Prostate volume >60 cm^3: 24	205± 43* 201 ±47* 232 ±48*	- - -	3.3 ± 2.2 3.2 ± 2.2 3.1 ± 1.5
Skolarus, 2010[a] [91]	University of Michigan Health System, Ann Arbor، MI, USA	Prostate volume <50 cm^3: 582 Prostate volume 50–100 cm^3: 279 Prostate volume >100 cm^3: 24	232* 248* 250*	- - -	- - -
Huang, 2011[a] [92]	Harvard Medical School, Boston, MA, USA	Prostate size 24-41 g: 221 Prostate size 42-50 g: 221 Prostate size 51-62 g: 221 Prostate size > 62 g: 221	149.1 ± 39.3* 153.3 ± 40.5* 158.0 ± 40.1* 164.2 ± 48.4*	7.6 ± 3.2* 7.7 ± 2.8* 7.6 ± 2.3* 8.5 ± 4.3*	1.2 ± 1* 1.2 ± 0.7* 1.1 ± 0.5* 1.3 ± 1*
Our study [b]	Department of Urology and Pediatric Urology, University Hospital, Kiel, Germany.	Prostate volume <30 cm^3: 63 Prostate volume 30–49 cm^3: 121 Prostate volume 50–69 cm^3: 55 Prostate volume >70 cm^3: 27	288 ±53 287 ± 62 292 ± 51 301 ± 68	10.6 ±6.5* 10.8 ± 6.5* 9.4 ± 5.1* 14.9 ±14.7*	12.4 ±.8.4 11.8 ±5.7 11.5 ± 6.7 12.6 ± 7.1

[a] These studies are evaluating the impact of BMI on perioperative outcome after RALP. * Statistically significant
[b] One way ANOVA

5.2 Perioperative data

5.2.1 Pelvic lymph node dissection (PLND)

The most effective method for detecting LN metastases in PCa is PLND; this allows for appropriate staging, accurate predictions and can help to choose optimal post-surgical follow-up treatment, i. e. the choice between either adjuvant or salvage therapy [93]. PLND includes the removal of the nodes overlying the external iliac artery and vein, the nodes within the obturator fossa that are located cranially and caudally to the obturator nerve and the nodes medial and lateral to the internal iliac artery (Table 17) [94,95]. The advantage of PLND for improved staging and/or increased cancer curativity should be weighed against intraoperative and postoperative complications [93]. We routinely perform PLND in during each RP despite its supposed association with increased surgical time and the risk of complications; however, our data show no significant correlation between PLND, the incidence of complications and operative time (Spearman correlation Coefficient, $p = 0.062$ and 0.059 respectively).

Table 17: *Recommendation of German Urological Society regarding PLND in localized PCa [95].*

Recommendations / Statements	Grade of recommendation
Patients with PCa should be informed about the risk of LN metastasis and the advantages and disadvantages of lymphadenectomy. Total agreement: 98%	A
In patients with a low risk PCa (pT1c and PSA <10 and Gleason ≤ 6) a lymphadenectomy is not indicated. Total agreement: 91%	C
The more extensive the lymphadenectomy, the greater the chance of nodal positive findings. This allows for exact staging and early initiation of adjuvant therapy with proven LN metastases. Total agreement: 96%	Statement
If lymphadenectomy performed, at least 10 lymph nodes should be removed. Total agreement: 76%	B
Currently, there is no evidence that extended lymphadenectomy causes a survival benefit for nodal-positive or nodal-negative patients without adjuvant measures. However, there are indications that progression-free survival is influenced favorably. Total agreement: 87%	Statement

A Based on clinical studies of good quality and consistency that addressed the specific recommendations, including at least one randomised trial
B Based on well-conducted clinical studies, but without randomised clinical trials
C Made despite the absence of directly applicable clinical studies of good quality

5.2.2 Nerve-sparing RP

The development of nerve-sparing anatomic RP by Walsh and colleagues has led to improved potency rates, however the results regarding potency preservation published in the literature are not satisfactory [96]. A majority of surgeons agrees that the ideal candidate for a nerve-sparing procedure is a preoperatively fully potent patient with an organ-confined cancer, that is, a clinical $T_{1/T2a\text{-}b}$ disease [97].

Patients who underwent nerve-sparing procedures were more likely to have PSMs, as there is a significant yet weak positive correlation between nerve-sparing procedures and positive surgical margins (spearman correlations coefficient r = .154, p = .009 *"own data"*). These findings seem to be a logical consequence of nerve-sparing procedures and they are similar to other non-randomized trials (Table 18).

Table 18: *The correlations between nerves-sparing RP and positive surgical margin.*

First author	Institution		NSRP,%	non-NSRP,%	P value
Moore [98], 2011	St Vincent 's Hospital, Sydney, NSW, Australia	PSM			
		T2	12.3	21.4	.871
		T3	40.3	52.2	.028[*a]
		overall	19.4	38.6	
Alkhateeb[99], 2010	Margaret Hospital, University Health Network, University of Toronto,	PSM			
		T2	10.4	15.7	0.07
		T3	26.3	24.1	0.76
		overall	13.4	17.7	0.11
Our study[a]	Department of Urology and Pediatric Urology, University Hospital, Kiel, Germany.	PSM			
		T2	13.1	6.5	.258
		T3	17.4	30.4	.284
		overall	15.1	16.2	.009[*]

NSRP - Nerve sparing RP; PSM - Positive surgical margin
Fisher's exact test
* Statistical significant difference (P < 0.05)
[a] for T_{3a}

5.2.3 Operative time

The available literature suggests that the duration of RP procedures decreases with surgeon experience and skill [100]. The operating time was longer in RALP compared to RRP (331.3 vs. 269.5 min., *p < .0001,"own data"*), thus also in all publications due to docking time and learning curve. Our data show that procedures involving a large prostate tend to last longer (Table 16). However, the operative time seems to be not affected by LN discussion and nerve sparing procedures, BMI and pathological T stage, as insignificant correlations between operative time and those latter factors.

5.2.4 Hospitalization time

Several studies have demonstrated a shorter hospitalization time after RALP as compared with RRP (Table 19). A statistically significant difference between both groups was found for the length of hospital stay (mean 9.7 vs. 13.5 days, p < 0.001), in favor of RALP (Table 11). The variation in hospitalization time at different institutions may reflect differences in surgical volume or patient characteristics.

A longer hospitalization time was found in patients who had peri-operatve complications, as a significant weak-positive correlation was found between hospital stay and rectal injuries (Spearman correlation coefficient r = .169, p = 0.004); anastomotic insufficiency (Spearman correlation coefficient r = .291, p < 0.001); urinary tract infections (Spearman correlation coefficient r = .162, p = 0.006); lymphoceles (Spearman correlation coefficient r = - .145, p = 0.015); thrombo-embolic complications (Spearman correlation coefficient r = .255, p < 0.001) and a significant moderate positive correlation for SSIs (Spearman correlation coefficient r = .375, p < 0.001). However, there were insignificant correlations for many other complications, e.g hemorrhagic, urinary retention, illus and blood transfusion.

5.3 Oncologic outcomes

The pathological examination of the surgical specimen provides crucial information regarding prognostic factors that include tumour stage, Gleason score and surgical margin status.

5.3.1 Positive surgical margins (PSMs)

PSMs after RP are uniformly considered an adverse outcome associated with failure of the surgery to achieve cure of the PCa [101]. Our data shows that patients who underwent RALP were more likely to have negative surgical margins; a statistically significant difference between both groups was found with respect to PSMs, the outcome in negative surgical margins was in favour of RALP (78.8% vs. 63.4%, p < *0.001*).

Table 19 shows the perioperative parameters and the main complications rates in several studies comparing RRP and RALP. The outcome of this comparison demonstrates that the longer operating time in our study, which may be due to the fact that our operation time includes the anesthesia time which is around 30-40 min and in RALP the docking time takes about 20-30 min; in addition we have to take into account the learning curve as we only started RALP during this time. Moreover, the longer hospitalization time is also accredited to the fact that the patient is only discharged after removal of the urethral catheter and owed to German health insurance regulations. In his study from Dresden, Germany, Froehner et al, 2013 shows that the mean hospitalization time in RRP was 7.7 days and in RALP 8 days, while in Kiel the duration was 13.5 vs. 9.7 days in RRP and RALP respectively [102].

In current data, the complications rates seem to be higher (RRP 62% vs. RALP 38.8%) than in the other studies despite excluding the possibility of duplicated numbers as many patients had more than one complication; we considered only the worst one according to the modified Clavien- Dindo Classification. On the other hand, Wallerstadt *et al.*, 2015 showed the complication rates of RRP to be 80.5% vs. RALP 70.1% in a large multi-centers study [103]. The outcome after RP, including perioperative , oncologic and Health-Related Quality of Life (HRQL), is multi-factorial due to different patient and tumor characteristics as well as the surgeons' experience and surgical technique.

Table 19: *Perioperative, oncological outcomes and complications rates in the studies compare RRP and RALP.*

First author	Institution	No. of cases, type	Mean age, y	BMI	Preoperative PSA ng/mL, median	Mean Prostatic vol, cm3!	Median/mean operative time, min	HB loss g/dl	Hospitalization time, days
Menon[104], 2002	Vattikuti Urology Institute, Henry Ford Health System, Detroit, Michigan;	RRP 30	64	30	8,4*	48.4	138*	4.4*	2.3*
		RALP 30	62	30	9.94*	58.8	288*	1.2*	1.5*
Tewari[105], 2003	Vattikuti Urology Institute, Henry Ford Health System, Detroit, Michigan;	RRP 100	63.1	27.6	7.3	48.4	163	-	3.5*
		RALP 200	59.9	27.7	6.4	58.8	160	-	1.2*
Ahlering[106], 2004	Department of Urology, University of California Irvine, Medical Center, Orange, California	RRP 60	62.7	26.5	8.4	50.7	214	3.3*	2.2*
		RALP 60	62.9	26.3	8.1	52.5	231	1.6*	1.1*
Nelson[107], 2007	Department of Urologic Surgery, Vanderbilt University Medical Center, Nashville, Tennessee	RRP 374	59.9	-	8.4	-	-	-	1.23
		RALP 629	59.3	-	6.7	-	-	-	1.17
Smith[108], 2007	Department of Urologic Surgery, Vanderbilt University Medical Center, Nashville, Tennessee	RRP 200	61.1	27.8	8.3*	43.9*	-	-	-
		RALP 200	60.3	28.5	6.4*	53*	-	-	-
Fracalanza[109], 2008	Departments of Oncological and Surgical Sciences, Urology Clinic,	RRP 26	68.5*	26.4	6.2	36	127.2*	-	8*
		RALP 37	62*	25.5	6.2	40	195.6*	-	5*
Ficarra, [110], 2008	Department of Oncological and Surgical Sciences, Urology Clinic, University of Padua, Padua, Italy	RRP 105	65*	26	6	40	-	-	-
		RALP 103	61*	26	6.4	37.5	-	-	-
Krambeck[111], 2009	Departments of Urology and *Division of Biostatistics, Mayo Medical School and Mayo Clinic, Rochester, MN, USA	RRP 588	61	-	5	-	-	-	-
		RALP 294	61	-	4.9	-	-	-	-
Hohwü[112], 2009	Multi- centers	RRP 147	56	26.9	11.7	-	-	-	-
		RALP 127	57.9	25.9	7.7	-	-	-	-
Mirza[113], 2011	Department of Urology-MS 3016, University of Kansas Medical Center, 3901 Rainbow Boulevard, Kansas City, USA	RRP 180	61.7	-	8.9*	-	-	-	2.28*
		RALP 191	60.1	-	6.7*	-	-	-	1.23*
Ryu[114], 2013	Department of Urology, Asan Medical Center, University of Ulsan College of Medicine, Seoul Korea	RRP 340	64.9	24.7	9.7	36.2	170.8	-	10.1*
		RALP 524	64.9	24.6	10.1	36	146.4	-	7.9*
Froehner[102], 2013	Departments of a Urology University Hospital 'Carl Gustav Carus',	RRP 2,438	64.9*		10.4*	-	-	-	7.7
		RALP 317	62.6*		6.4*	-	-	-	8.0
Sammon[115], 2013	Multi- centers	RRP 28,054	-	-	-	-	-	-	-
		RALP 49,562	-	-	-	-	-	-	-

Vora [116], 2013	Multi- centers	RRP 95	60.3		9.1	-	-	-	--
		RALP 140	62.1		8.3	-	-	-	--
Alemozaffar[117], 2014	Department of Urology, Emory University School of Medicine, Atlanta, GA, USA;	RRP 621	65.4*	26.0*	5.6*	52.6	-	-	2.9*
		RALP 282	67.2*	26.4*	5.0*	55.8		-	1.8*
Gagnon[118], 2014	The Vancouver Prostate Centre and Department of Urologic Sciences, University of British Columbia, Vancouver, BC	RRP 200	64.7	27.2	11.2	35.2	114.2*	-	2*
		RALP 200	64.2	27.2	6.6	36.9	233.6*	-	1.7*
Wallerstadt[103], 2015	Multi- centers	RRP 778	63	26.2	6.2	-	103*	-	4.1*
		RALP 1847	63	25.9	6.1	-	175*	-	3.3*
Our study	Department of Urology and Pediatric Urology, University Hospital, Kiel, Germany.	RRP 187	67.7	27.3	8.7*	41.6	269.5*	4.4	13.5*
		RALP 98	68.1	26.8	7.4*	45.4	331.3*	3.9	9.7*

*$p < 0.05$

! Pre or postoperative prostatic volume

Table 19: *(Cont.)*

First author	No. of cases, type	Transfusion rate, %	Catheterisation duration, d	Overall PSM, %	Overall complication rate, %
Menon[104], 2002	RRP 30	17*	13.7*	29	36.7
	RALP 30	7*	10.7*	26	26.7
Tewari[105], 2003	RRP 100	67*	15.8*	23*	20*
	RALP 200	0*	7*	6*	2.5*
Ahlering[106], 2004	RRP 60	2	9	12	10
	RALP 60	0	7	16.7	6.7
Nelson[107], 2007	RRP 374	-	-	-	15
	RALP 629	-	-	-	17
Smith[108], 2007	RRP 200	-	-	35.5*	-
	RALP 200	-	-	15*	-
Fracalanza[109], 2008	RRP 26	-	-	23	-
	RALP 37	-	-	28.6	-
Ficarra, [110]2008	RRP 105	-	-	-	13
	RALP 103	-	-	-	10
Krambeck[111], 2009	RRP 588	-	-	38.1	-
	RALP 294	-	-	32.7	-
Hohwü[112], 2009	RRP 147	-	-	-	-
	RALP 127	-	-	-	-
Mirza[113], 2011	RRP 180	-	-	28.9	-
	RALP 191	-	-	13.6	-
Ryu[114], 2013	RRP 340	42.2*	7.5*	-	68
	RALP 524	6.3*	6.2*	-	27.3
Froehner[102], 2013	RRP 2,438	10.4	-	-	45.3
	RALP 317	8.9	-	-	24
Sammon[115], 2013	RRP 28,054	-	-	-	12.7
	RALP 49,562	-	-	-	8.6
Vora [116], 2013[a]	RRP 95	-	--	58.9	-
	RALP 140	-	--	47.1	-
Alemozaffar[117], 2014	RRP 621	30.3*	-	23.1	-
	RALP 282	4.3*	-	24.5	-
Gagnon[118], 2014	RRP 200	1.5	-	31	11.5*
	RALP 200	3.5	-	24.6	22*

Wallerstadt[103], 2015	RRP 778	-	-	-	80.5*
	RALP 1847	-	-	-	70.1*
Our study	RRP 187	7.1	12.6*	36.6*	59.9*
	RALP 98	6.1	9.2*	21.4*	39.8*

*$p < 0.05$
[a] for locally advanced PCa

5.4 Complications.

Many complications have been reported after RP with an overall intra- and postoperative incidence of 54% (own data). The complications were as follows:

5.4.1 Intraoperative vascular injuries

Vascular injuries are a potentially devastating complication of RP. They may occur in the initial stages of the operation, such as when gaining access to the abdominal cavity in RALP and LRP, or during PNLD. The most common intraoperative problem is bleeding, usually arising from venous structures and the key to avoiding them is through careful dissection and by avoiding tunnel-like operating fields limiting visualization and access to surrounding structures. It is important to recognize such injuries promptly and to manage them immediately [119–121]. The incidence of detected intraoperative vascular injuries in our data was 1.1%; 3 cases who underwent RALP were managed intraoperatively by hemostatic suture without open conversion and/or postoperative problems.

5.4.2 Rectal injury

Regardless of the approach, rectal injury is a possible complication of RP because of the close anatomical relationship between the rectum and the prostate [122]. The incidence of rectal injury ranges between 0.7 and 2.4%. Intraoperative detection and repair of the injury is crucial [67]. Multi-layered primary closure and interposition of omentum between the rectum and anastomosis with or without proximal ileostomy usually avoids long-term problems [119]. The incidence of rectal injury in our study was 1.4%; two cases (one case for each RALP and RRP) were discovered intraoperatively and treated with primary closure and safety proximal iliostomy and other two cases of RRP incomplete rectal injury was discovered intraoperatively and treated only with primary closure and postoperative total parenteral nutrition.

5.4.3 Anastomotic insufficiency or prolonged catheterization time

Failure to achieve a watertight closure of the anastomosis can result in urinary extravasations and accumulation of urine, even if a pelvic drain is placed [67]. The catheter may be removed 3 to 21 days after surgery, depending on the integrity and the amount of tension on the vesico-urethral anastomosis, its removal before 7 days is associated with a 15% to 20% risk of urinary retention. After the catheter has been removed, Kegel exercises should be initiated and a protective pad used until complete urinary control is achieved [56]. On the 7th postoperative day, a cystogram was performed to evaluate the vesico-urethral anastomosis in both RRP and RALP cases; if there was no leakage in the cystogram, the catheter was removed. Table 20 demonstrates the different postoperative periods after which the catheter was removed and the correlating number and percentage of cases in RRP and RALP.

Table 20: The number and percentage of the our cases by which the catheter was removed different postoperative days

Catheterization time	RALP,%	RRP,%	P Value
7 days or less	73 (76%)	89 (48.4%)	< .0001
8 to 10	7 (7.3%)	26 (14.1%)	
11 to 14	0	17 (9.2%)	
15-21	11 (11.5%)	30 (16.3%)	
>21	5 (5.2%)	22 (12%)	

Fisher's exact test * Statistical significant difference (P < 0.05)

Anastomotic insufficiency is usually treated by prolonged catheterization; 45 patients (15.8%, 10 cases RALP and 35 cases RRP) were treated with prolonged catheterization of up to 36 days in RALP and 69 days in RRP. In some rare cases, leakage requires more invasive intervention such as bilateral percutaneous nephrostomy (PCN) or urethra-cystoscopy (UC) to evaluate the anastomotic area; PCN and UC were done in one RRP patient each.

5.4.4 Hemorrhagic (delayed bleeding) complications

Significant bleeding after RP is defined as postoperative hemorrhage requiring acute transfusion of blood to support blood pressure; a patient who requires acute transfusions for hypotension after RP within the pelvis should be explored to evacuate the pelvic hematoma to decrease the risk of bladder neck contracture and incontinence [119]. The incidence of postoperative hemorrhagic complications was 1.4% *"own data"* (4 cases: 3 RALP and one RRP). These patients presented with postoperative bleeding and pelvic or retroperitoneal hematoma that needed immediate surgical evacuation under general anesthesia ± bilateral immobilization of the internal iliac arteries. One RALP patient presented with a subcutaneous hematoma and small pelvic hematoma, which was treated conservatively.

5.4.5 Postoperative voiding difficulties

Urethral stricture formation is a known complication of RP with a reported incidence of 0.4% to 32%. These strictures most commonly occur at the bladder neck and arise from inadequate approximation during surgery, urinary extravasation, or distraction of the bladder neck from a hematoma; this causes should be considered in any patient who complains of a poor urinary stream or in patients who have prolonged and unaccountable incontinence [119,123]. Two patients (0.7%, one case in RRP and RALP each) developed micturition difficulties within 3 months postoperatively; they were treated by transurethral resection of the anastomotic area under general anesthesia.

5.4.6 Lymphoceles

A lymphocele, also known as a lymphocyst, is a collection of lymphatic fluid occurring in consequence of surgical dissection and inadequate closure of the afferent lymphatic vessels. PLND is a technically challenging surgery and can be associated with higher rates of intra- and/ or postoperative complications. Lymphoceles are the most frequent postoperative complications after PLND and the risk of lymphocele development is usually affected by the extent of PLND and by the choice of surgical access (transperitoneal or extraperitoneal) [124].

Lymphoceles are often incidentally found during routine sonographic examination; however they may also cause clinical symptoms. The point of necessary intervention is still not clearly defined and asymptomatic lymphoceles usually do not require drainage or treatment; larger of lymphoceles may compress the bladder or the external iliac vein and infected lymphoceles may also need treatment. Percutaneous drainage with or without injection of a sclerosing agent, or laparoscopic opening of a window with marsupialization of the lymphocele are typically successful measures [67].

Despite the extraperitoneal access of the RRP with standard peritoneal fenestration to avoid lymphoceles, 34 patients (11.9%, 26 RRP and 8 RALP cases) presented with postoperative lymphoceles. 18 cases (6.3%, 15 RRP and 3 RALP cases) were treated by laparoscopic peritoneal fenestration, 6 cases (3 RRP and 3 RALP cases) were treated by US- / CT- guided pig tail insertion (drain) and 10 cases (3.5%, 8 RRP and 2 RALP cases) were treated by conservative management.

5.4.7 Thrombo-embolic complications

Thrombophlebitis with pulmonary embolism is a life-threatening complication and a major cause of mortality after RP. A recent population-based report estimated the rates of thrombo-embolic events after RP between 2.9% and 3.9% irrespective of the surgical approach and despite routine use of prophylaxis, it is still associated with a substantially higher risk of mortality than other complications [125,126] . Several risk factors increase thrombo-embolic events after RP such as advanced age, comorbidities like cardiopulmonary disease, a prior history of DVT, more advanced PCa and simultaneous PLND [127].

Measures to prevent this complication include careful positioning on the operating room table to avoid compression of the veins in the lower extremity, early ambulation and low-dose low-molecular-weight heparin which is used at some centers. Most importantly, patients should be informed of the potential signs and symptoms of this complication before they go home and should be instructed to call the physician immediately if they have any of the following symptoms: swelling or pain in the leg, especially in the calf; sudden chest pain thatworsens on taking a deep breath; hemoptysis; shortness of breath; or a sudden onset of weakness or fainting [119]. In our study, five cases (1.8%) developed postoperative thrombo-embolic complications, one RRP case developed massive pulmonary embolism postoperative and was admitted in ICU. Two RRP cases developed postoperative DVT, which was treated by anticoagulant therapy and two cases (RRP and RALP one each) developed a postoperative cerebral stroke, which was treated by anticoagulant therapy with development of neurological affections.

5.4.8 Urinary tract infections

Urinary tract infections (UTIs) together with pneumonia are most common type of healthcare-associated infection, after SSIs and account for more than 15 % of infections reported by acute care hospitals [128]. Urinary tract infections can manifest as bacteriuria with limited clinical symptoms, sepsis or severe sepsis, depending on localised or systemic extension [129].

Criteria for postoperative urinary tract infections (UTI) vary by organization, medical specialty and even within hospitals. However, in AUA white paper for catheter-associated urinary tract infections show the definitions and symptoms must be present in the patient to meet the diagnosis (Table 21) [130]. In our study, seven cases (2.5%, 2 RALP and 5 RRP cases) showed a positive urinary culture of $>10^5$ colonies/mL urine and were treated with intravenous antibiotics.

Table 21: *Postoperative symptomatic urinary tract infection must meet one of the following two criteria [130].*

One of the following: fever (>38°C), urgency, frequency, dysuria, or suprapubic tenderness	And	Urine culture of >105 colonies/mL urine with no more than two species of organisms
Two of the following: fever (>38°C), urgency, frequency, dysuria, or suprapubic tenderness	And	Any of the following: • Dipstick test positive for leukocyte esterase and/or nitrite • Pyuria (>10 WBCs/mL or >3 WBC/hpf of unspun urine) • Organisms seen on Gram stain of unspun urine • Two urine cultures with repeated isolation of the same uropathogen with >102 colonies/mL urine in non-voided specimen • Urine culture with <105 colonies/mL urine of single uropathogen in patient being treated with appropriate antimicrobial therapy • Physician's diagnosis • Physician institutes appropriate antimicrobial therapy

5.4.9 Surgical site infections

SSI the most common type of healthcare-associated infections; its morbidity is not limited to the physical discomfort of the wound, impaired cosmetics, or prolonged time to recovery. Patients who develop an SSI are about 60% more likely to spend time in an intensive care unit, 5 times more likely to be readmitted to the hospital or to have longer hospitalizations, substantial increases in costs of care and twice more likely to have the incidence of a 30-day mortality than patients who do not develop an SSI [131,132].

In his 2011 paper, Tollefson shows that patients undergoing RARP had lower rates of SSI than similar patient cohorts undergoing RRP (0.6% vs. 4.7%; *P= .001*) [132]. In our study, 19 patients (6.7%) developed SSIs (17 RRP and 2 RALP cases). Of these, 13 (4.6%) RRP cases developed postoperative SSI and wound dehiscence (deep incisional SSIs), which were treated by repeated changing of the Vacuum Assisted Closure system (VAC), three cases (1.1%, one RRP and two RALP cases) developed infected lymphoceles (space / organ SSIs) that were treated either with CT / US-guided pig tail insertion or surgical evacuation and lavage and three RRP cases (1.1%) developed postoperative SSIs that could be treated with local measures (superficial incisional SSI).

5.4.10 Postoperative ileus

Postoperative ileus is a frequent complication of abdominal surgery and is defined as a temporary impairment of gastrointestinal motility after surgery. Despite the advances in surgical techniques and preoperative care for abdominal pathologies, postoperative ileus is a common complication after abdominal surgery [133]. Although the results of post-RP ileus vary, the incidence ranges from 5–25% thus prolonging the duration of the hospital stay, reducing patient satisfaction and increasing the overall costs [134]. The postoperative ileus is traditionally accepted as a physiological response to abdominal surgery, although several etiologies, such as physiological response to surgical trauma, visceral manipulation, intra– and/or postoperative complications and postoperative opiate usage [134].

The point at which the postoperative ileus becomes abnormally prolonged has not been clearly established. It normally resolves within approximately four days after an abdominal surgical procedure; however, it may last 2 days or less following laparoscopic surgery and may continue for more than one week after major laparotomies [135]. In our study, 6 cases (2.1%, 4 RRP and 2 RALP cases) developed a post postoperative ileus that lasted more than 4 days and could only be resolved by medical treatment.

5.4.11 Blood or fresh frozen plasma transfusion

RP is associated with an elevated potential for intraoperative blood loss that may lead to the necessity for blood transfusion. The transfusion rates at tertiary care centers range from 3% to 67%, irrespective of the transfusion type and surgical approach [136]. However, the shift from RRP to minimally invasive RP may result in fewer bleeding complications thereby reducing the overall need for blood transfusions; however a significant blood loss during RP remains problem [137,138]. The incidence of postoperative transfusion of packed RBCs and FFP was

20 cases (7%, 14 RRP and 6 RALP) which needed postoperative transfusion either of erythrocyte concentrate, FFP and/or platelet concentrate, ranging from 2 to 10 units of erythrocyte concentrate.

5.4.12 Ureteral injury or stricture

Ureteral injury or stricture is an uncommon complication. It is more likely to occur in patients with a large prostate, a prior history of prostatitis, a large median lobe, previous prostate procedures and it can occur both as intravesical ureteral injury, i. e. during dissection of the posterior bladder neck or as extra-vesical ureteral injury, i. e. during lateral dissection of the peritoneal reflection for creation of the extra-peritoneal space; in addition, the ureter may be injured as it might be mistaken for the vas deferens and less commonly, it could be e injured during PLND [139].

Prevention of ureteral injury is best accomplished by careful identification of anatomic landmarks and template-oriented systematic PLND with defined boundaries and through pre- or intraoperative placement of ureteral catheters for patients who are at risk for ureteral injury. Furthermore, cystoscopic examination can be used to delineate the bladder neck and the ureteral orifice anatomy in patients with large median lobes during or prior RP [140,141]. In our study, he incidence of ureteral injury and postoperative ureteral stricture was two cases (0.7%, both RRP), one occurred intraoperatively as a ureteral injury due to marked retroperitoneal fibrosis and was treated by primary closure and insertion of a JJ stint, which was removed one month after the operation and in the other case the patient developed a ureteral stricture two months postoperatively requiring re-exploration and re-implantation of the ureter into the bladder.

5.4.13 Conversion to an Open Procedure

Converting from a minimally invasive approach to an open procedure should not be considered a complication it itself, but the conversion is more likely to be performed in the presence of a complication [139]. Open conversion is rare (<2%) and has been cited in the literature as occurring usually during a surgeon’s early experience with LRP or RALP, mainly as a result of a failure to progress or uncertainty of dissection planes. The patient must be informed about this possibility [142]. Appropriate judicious decision-making regarding open conversion can actually prevent a complication. In our study, open conversion occurred only in one case (0.35%) during the early learning curve and in a 2nd patient due to intraoperative technical difficulties, bleeding and rectal injury.

5.4.14 Death

Death after surgery is a clinically important outcome measure for surgeons, patients, policy-makers and health-service researchers and is increasingly being used as an indicator of quality for major surgical procedures [143]. Death within 30 days after RP is relatively uncommon and occurs in <1% of patients; it is affected by the age of the patient and possible comorbidities. The most common causes of death are cardiovascular events, such as myocardial infarction and pulmonary embolism [144,145]. In our series, two patients (0.7%, both RRP) died during the early postoperative course: one died on the first postoperative day due to cardiogenic shock and the other died within the first two postoperative weeks due to massive pulmonary embolism.

5.5 Learning curve.

Despite the learning curve of our surgeons, the perioperative outcome of RALP was more favorable than that of RRP; the patients who underwent RALP had shorter catheterization and hospitalization times and lower overall complications rates, as well as lower rates of anastomotic insufficiency, lymphoceles and SSIs. Moreover, our RALP results are comparable to most other contemporary series (Table 22).

In order to evaluate the learning curve of RALP, we compared the perioperative outcome of the initial 50 cases (Group I) and the subsequent 48 cases (Group II). Here we found a clear decrease in the mean operating time (340.7 ± 59.4 vs. 321.5 ± 53.5 min., $p = .192$), catheterization time (9.3 ± 5.5 vs. 9.1 ± 5.6 days, $p = .931$) and a significant decrease in hospitalization time (10.2 ± 4.2 vs. 9.1 ± 2.3 days, p = .038).

The absence of standardized reporting of surgical complications for RP lead to a wide variation in the types of complications reported as well as in the overall incidence of complications. In Table 22, we try to summarize the incidence of various complications in studies comparing RRP and RALP. From this Table we may conclude that the incidence of perioperative complications in our patients was comparable with others in the literature, e. g. rectal injury and UTIs, however, there was a greater tendency for postoperative lymphceles and SSIs in RRP patients and lesser tendency for postoperative urinary difficulties and ileus.

Several authors have started using the Clavien- Dindo classification system to describe complications associated with minimally-invasive RP [71]. In Table 23 we compare our complications results with respect to the Clavien classification to those of other studies comparing RRP and RALP. The comparison shows our patients to be more likely to have major complications than other studes, especially grade IIIb patients in both groups.

Table 22: *Incidence of various complications in the studies compares RRP and RALP.*

First author	No. of cases, type	Vascular injuries, %	Rectal injury, %	Uretric injury or stricture, %	Urinary leakage, %	Hemorrhagic complications, clot retention %	Postoperative infection fevers, %	Lymphocele, %	Ileus, %	Thrombo-embolic complication, %	SSIs, %	Open Conversion, %	Postoperative urinary difficulty, or retention %	Death,%	Overall complication rate, %
Menon[104], 2002	RRP 30	-	3	-	-	-	-	-	9	-	1	-	3	0	36.7
	RALP 30	-	0	-	-	-	-	-	9	-	1	3	3	0	26.7
Tewari[105], 2003	RRP 100	-	1	-	-	4	4*	2	3	2	1	-	-	-	20*
	RALP 200	-	0	-	-	0.5	-	0	1.5	0.5	1	0	-	-	2.5*
Nelson[107], 2007	RRP 374	-	0	-	1	1.2	2.1	1.4	4.1	0.5	1.4	-	1	-	15
	RALP 629	-	0.15	-	2.4	2	2.3	0.3	4.2	1.15	0.3	-	0.3	-	17
Ficarra, [110]2008	RRP 105	-	0	-	-	7	-	-	1	2	1	-	-	-	-
	RALP 103	-	2	-	-	7	-	-	1	0	0	-	-	-	-
Krambeck[111], 2009	RRP 588	-	-	0.2	-	1.8	1.3	1.9	-	4.2	-	-	7.7	-	-
	RALP 294	-	-	0	-	3.5	1	1.1	-	2	-	-	7.9	-	-
Ryu[114], 2013	RRP 340	-	-	-	10*	-	-	-	-	-	4.1*	-	7*	-	-
	RALP 524	-	-	-	2.1*	-	-	-	-	-	0.2*	-	2.7*	-	-
Froehner[102], 2013	RRP 2,438	-	-	-	-	-	-	26.1*	-	3.2	3.2	-	-	0.04	45.3
	RALP 317	-	-	-	-	-	-	30.9*	-	2.5	2.5	-	-	0.3	24
Sammon[115], 2013	RRP 28,054	-	-	-	-	-	-	-	-	-	-	-	-	0.1	12.7
	RALP 49,562	-	-	-	-	-	-	-	-	-	-	-	-	0	8.6
Wallerstadt[103], 2015	RRP 778	-	-	-	-	13.8	12.6	-	11.2	2.8	5.6	-	-	-	80.5*
	RALP 1847	-	-	-	-	11.8	15.3	-	7.8	0.6	3.3	-	-	-	70.1*
Our study	RRP 187	0	1.6	1.2	20	0.5	3.2	13.9	2.2	2.2	9.2	-	0.5	1	59.9*
	RALP 98	3.1	1	0	10.2	4	2	8.1	2	1	2	1	1	0	39.8*

Table 23: *The percentage Clavien classification system of complications in the studies compares RRP and RALP.*

First author	No. of cases, type	I, %	II, %	IIIa, %	IIIb, %	IV, %	V, %
Ryu[114], 2013	RRP 340	16.1	44.4	2.9	4.4	0.3	-
	RALP 524	16	7.8	2.1	0.8	0.6	-
Gagnon[118], 2014	RRP 200	5.5	3	2	1	0	0
	RALP 200	13	7	1.5	0.5	0	0
Our study	RRP 187	25.7	11.8	2.1	18.1	1.1	1.1
	RALP 98	18.4	8.1	5.1	7.1	0	0

6. Summary and conclusion:

The DaVinci robotic surgery system offer numerous advantages providing improved visualization, increased dexterity, restored proper hand-eye coordination, ergonomic work position of the surgeon and it offers 3D images with 12-fold magnification. This provides a mode of vision allowing for meticulous dissection procedures. As the camera is controlled by the surgeon, he/she can maintain a stable, optimal view of the surgical field without concern for the camera-driver. This study represents a retrospective case series of patients who were treated with RP, either RRP or RALP) for a confirmed PCa over the last 4 years in the Department of Urology and Pediatric Urology of the University Hospital Schleswig-Holstein, Campus Kiel, Germany. 285 patients were included in this study, 98 of these were treated with RALP and 187 with RRP. In January 2013, the first cases of RALP were performed and from that time the majority of patients underwent RALP as the patient numbers undergoing RRP decreased rapidly down to only five cases in 2014 and no cases in 2015.

The age of the patients included in this study was 68.1 ± 6.7 years (range: 47-85), BMI 27.2 ± 3.8 kg/m^2 (range: 19.5-42.4) and the preoperative prostate size was 42.9 ± 21.2 cm^3 (range: 12-160). Patients who underwent RALP were more likely to have nerve sparing procedures (82.7% vs. 47.1%, $p < .0001$). However, the operating time in these patients was longer (331.3 min. vs. 269.5 min, $p < .0001$). The oncological data show that more than 50% of the patients who underwent RP had a pathological tumor stage (pT2) and the patients who underwent RALP were less likely to have metastases in the LN drainage system or positive surgical margin. The overall complication rate was 54% (154/285) and despite the learning curve of our surgeons patients who underwent RALP were less likely to have complications (39%, 38/98) compared to those who underwent RRP (62%, 115/187) and had a lower incidence of anastomotic insufficiency and SSIs than RRP patients, however they were more prone to haemorrhagic complications. The Clavien- Dindo Classification is an acceptable classification system to assess RP complications and it can be applied in our department not only for RP but also for all other surgical procedures. According to the Clavien- Dindo classification, the patients who underwent RALP were less likely to have minor complications than those with RRP (I 18/98 vs. 48/187; II 8/98 vs. 22/187) as well as major complications (III 12/98 vs. 38/187; IV 0/98 vs. 2/187 and V 0/98 vs. 2/187).

In conclusion:

Our study shows that the short-term perioperative outcomes and complications of RP may be influenced by the applied surgical technique. RALP and RRP remain acceptable options for treatment of PCa. Taken together; our findings with colleagues' published data show RALP to be an acceptable alternative to RRP with a lower risk of complications. However, patient characteristics and surgical experience are likely to impact the perioperative outcome and complication rates.

7. References

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ACKNOWLEDGEMENTS

Firstly, I'd like to sincerely thank almighty **ALLAH** for all his grants that he bestowed on me.

I would like to express my deepest gratitude to my advisor, **Prof. Dr Klaus- Peter Jünemann**, for the continuous support of my research, for his patience, motivation, and immense knowledge. His guidance helped me in all the time of research and writing of this thesis. I could not have imagined having a better advisor and mentor for my research.

Besides my advisor, I would like to thank **Dr. Osmonov**, who as a good friend was always willing to help, give his best suggestions and provided me an opportunity to join his team, and who gave access research facilities. Without they precious support it would not be possible to conduct this research.

I would like to take this opportunity to thank my **colleagues** in department of urology and pediatric Kiel University for their friendly attitude and the support they gave me when I needed it.

I would like to pay special thankfulness, warmth and appreciation to all **staff member in Urology department**, Assuit University Hospital, Egypt, for their encouragement and support, which I learned a lot from you in my clinical and surgical skills.

Warm thanks goes to my elderly sister Dr**. Hala Abou Faddan**, department of Public Health and Community Medicine, Assiut University, for her professional help in the statistical analysis of our data.

I'd like to present my sincere thankfulness to my **dear father** and my **deceased mother**, who died September 2013, for their great role in my life and their numerous sacrifices for me and for my sisters and brother. Many thanks for my sisters **Hala**, **Nagla** and **Eman** and my brother **Mohamed** for their support, encouraging me with their best wishes and for being truly siblings when needed.

Last but not least, I'd like to express my deepest gratitude to my beloved, my wife, **Sally Hussein** for her patience and tolerance over the last four years. **Sally** I could not be able to finish this work without your support. Thank you for being with me and for your appreciated sacrifices.

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PAPLICATION:

1- Shalaby MM, **Faddan AA**, Khalil M, Abdelhafez MF. April 2014. The management of the persistent Müllerian duct syndrome. Arab J Urol.

2- **Faddan AA**, Jünemann KP, Osmonov DK. In press. Semi-rigid penile prosthesis as salvage management of idiopathic ischemic stuttering priapism. Res Rep Urol.

3- **Faddan AA**, Jünemann KP, Osmonov DK. February 2016. Benchmarks for Partial Segmental Thrombosis of the Corpus Cavernosum: A Case Report and Review of the Literature.

4- Osmonov DK, , Naumann CM, Hamann MF, **Faddan AA**, Jünemann KP. September 2016. Cancer-specific and overall survival in patients with recurrent prostate cancer who underwent salvage extended pelvic lymph node dissection.

TRAINING PROGRAMS FOR DEVELOPMENT MY CAREER

- International Publishing of Research training program at Faculty and Leadership Development Center, Assuit University, 10th – 12th April, 2010.
- Strategic Planning training program at Faculty and Leadership Development Center, Assuit University, 17th – 19th April, 2010.
- Conference Organization training program at Faculty and Leadership Development Center, Assuit University, 26th – 28 th April, 2010.
- How to Compete for a Research Fund training program at Faculty and Leadership Development Center, Assuit University, 15th – 17th May, 2010.
- Student Evaluation training program at Faculty and Leadership Development Center, Assuit University, 22th – 24th May, 2010.
- Effective presentation training program at Faculty and Leadership Development Center, Assuit University, 12th – 14th June, 2010.